

## Abdominal compartment syndrome in patients with severe acute pancreatitis in early stage

Hong Chen, Fei Li, Jia-Bang Sun, Jian-Guo Jia

Hong Chen, Fei Li, Jia-Bang Sun, Jian-Guo Jia, Department of General Surgery, Xuan Wu Hospital of Capital Medical University, Beijing 100053, China

**Author contributions:** Chen H and Li F conceived and designed the study; Chen H acquired the data; Chen H, Li F and Jia JG analyzed and interpreted the data; Chen H and Li F drafted the manuscript; Li F, Sun JB and Jia JG critically revised the manuscript for important intellectual content; Li F and Sun JB supervised and was responsible for all aspects of the study.

**Correspondence to:** Dr. Hong Chen, Department of General Surgery, Xuan Wu Hospital of Capital Medical University, Beijing 100053, China. [chenhong@medmail.com.cn](mailto:chenhong@medmail.com.cn)

Telephone: +86-10-83198899-8463 Fax: +86-10-63037023

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### Abstract

**AIM:** To study retrospectively the influence of intra-abdominal hypertension (IAH) and abdominal compartment syndrome (ACS) in patients with early acute pancreatitis (AP) (during the first week after admission) on physiological functions, and the association of the presence of IAH/ACS and outcome.

**METHODS:** Patients ( $n = 74$ ) with AP recruited in this study were divided into two groups according to intra-abdominal pressure (IAP) determined by indirect measurement using the transvesical route *via* Foley bladder catheter during the first week after admission. Patients ( $n = 44$ ) with IAP  $\geq 12$  mmHg were assigned in IAH group, and the remaining patients ( $n = 30$ ) with IAP  $< 12$  mmHg in normal IAP group. For analysis of the influence of IAH/ACS on organ function and outcome, the physiological parameters and the occurrence of organ dysfunction during intensive care unit (ICU) stay were recorded, as were the incidences of pancreatic infection and in-hospital mortality.

**RESULTS:** IAH within the first week after admission was found in 44 patients (59.46%). Although the APACHE II scores on admission and the Ranson scores within 48 h after hospitalization were elevated in IAH patients in early stage, they did not show the statistically significant differences from patients with normal IAP within a week after admission ( $16.18 \pm 3.90$  vs  $15.70 \pm 4.25$ ,  $P = 0.616$ ;  $3.70 \pm 0.93$  vs  $3.47 \pm 0.94$ ,  $P = 0.285$ , respectively). ACS in early AP was recorded in 20 patients (27.03%). During any 24-h period of

the first week after admission, the recorded mean IAP correlated significantly with the Marshall score calculated at the same time interval in IAH group ( $r = 0.635$ ,  $P < 0.001$ ). Although ACS patients had obvious amelioration in physiological variables within 24 h after decompression, the incidences of pancreatic infection, septic shock, multiple organ dysfunction syndrome (MODS) and death in the patients with ACS were significantly higher than that in other patients without ACS (pancreatic infection: 60.0% vs 7.4%,  $P < 0.001$ ; septic shock: 70.0% vs 11.1%,  $P < 0.001$ ; MODS: 90.0% vs 31.5%,  $P < 0.001$ ; mortality: 75.0% vs 3.7%,  $P < 0.001$ ).

**CONCLUSION:** IAH/ACS is a frequent finding in patients admitted to the ICU because of AP. Patients with IAP at approximately 10-12 mmHg and early signs of changes in physiologic variables should be seriously considered for urgent decompression to improve survival.

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**Key words:** Acute pancreatitis; Abdominal compartment syndrome; Intra-abdominal pressure; Intra-abdominal hypertension; Organ dysfunction

**Peer reviewer:** Ibrahim A Al Mofleh, Professor, Department of Medicine, College of Medicine, King Saud University, PO Box 2925, Riyadh 11461, Saudi Arabia

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### INTRODUCTION

Compartment syndrome is a condition in which increased pressure in a confined anatomical space adversely affects circulation and threatens the perfusion of tissues therein. The abdominal cavity can be considered as a single compartment and any change in the volume of any of its contents will elevate intra-abdominal pressure (IAP). Abdominal compartment syndrome (ACS) is the clinical syndrome resulting from a persistent increase in IAP. Intra-abdominal hypertension

(IAH) contributes to organ dysfunction and leads to the development of ACS. The resultant ACS refers to the complications caused by elevated IAP, including diaphragmatic compression with reduced pulmonary compliance, cardiovascular and renal dysfunction, and intestinal and hepatic ischemia<sup>[1]</sup>. Recently, the elevated IAP after onset of acute pancreatitis (AP) has gained growing attentions. ACS is characterized by multiple organ dysfunction syndrome (MODS), and if unrelieved, eventually results in death. This study aims to investigate the incidence and clinical outcome of ACS in patients with AP in early stage (within the first week after admission).

## MATERIALS AND METHODS

### Criteria and definition

AP was diagnosed by the criteria based on the consensus of the international symposium on AP (Atlanta definition)<sup>[2]</sup>. The presence of IAH/ACS was defined by the criteria of the World Society of ACS (WSACS)<sup>[3]</sup>. The association between IAH and organ dysfunction characterized the ACS. IAH was defined as an IAP of 12 mmHg or higher, which often rendered many organs dysfunctional. IAH was a consistently increased IAP value of  $\geq 12$  mmHg recorded by at least three standardized pressure measurements during at least 8 h. ACS was diagnosed when the IAP exceeded 20 mmHg at which IAH caused severe physiologic derangements and associated with new, attributable single organ dysfunction or MODS. Septic shock was defined according to the American-European conference consensus definitions<sup>[4]</sup>.

### Patients

The study population included 74 patients with AP admitted to the surgical intensive care unit (SICU), Xuan Wu Hospital of Capital Medical University, from May 2002 to May 2006. General inclusion criteria for AP were defined as: (1) a time interval between onset of typical abdominal symptoms and study inclusion of 72 h and less; (2) the presence of systemic inflammatory response syndrome (SIRS) manifested by two or more of the following conditions: temperature  $> 38^{\circ}\text{C}$  or  $< 36^{\circ}\text{C}$ ; heart rate (HR)  $> 90$  beats/min; respiratory rate  $> 20$  breaths/min or  $\text{PaCO}_2 < 32$  mmHg; WBC count  $> 12\,000/\text{mm}^3$  or  $< 4000/\text{mm}^3$ , or  $> 10\%$  immature (band) forms; and (3) at least 3-fold elevated serum amylase or lipase levels, or a APACHE II score  $> 8$ , or a C-reactive protein (CRP) of  $\geq 250$  mg/L.

All patients were treated according to our standard management of pancreatitis protocol and the practice guidelines in AP<sup>[5]</sup>. The patients recruited in this study were divided into two groups according to IAP determined during the first week after admission. Patients ( $n = 44$ ) with IAP  $\geq 12$  mmHg were assigned in IAH group, and the remaining patients ( $n = 30$ ) with IAP  $< 12$  mmHg in normal IAP group. Patients with IAH or ACS were treated by lowering IAP with promoting enterokinesia, and/or percutaneous abdominal decompression and drainage and/or

decompressive emergency laparotomy. A silastic covering was placed to achieve a pressure-free abdominal closure when decompressive laparotomy was performed. The definitive closure was performed within 5-7 d. In the setting of gallstone pancreatitis and evidence of common bile duct obstruction, urgent endoscopic retrograde cholangiopancreatography (ERCP) with sphincterotomy was indicated to remove the impacted stone.

### Anthropometric examination and measurement

Patients with AP admitted to SICU underwent intermittent measurement of IAP, recording of the clinical data and calculation of MODS scores by Marshall *et al*<sup>[6]</sup>. Since intravesical pressure (IVP) measurement had been described as a standard and validated technique of indirectly reflecting IAP and rapidly recognizing ACS<sup>[7]</sup>, urinary bladder pressure (UBP) was routinely measured in all AP patients in our study. In brief, the patient was placed in complete supine position with a Foley catheter. One end of a transducer was connected to the Foley catheter through 3-way stopcocks. The monitor was zeroed with the transducer at the level of the symphysis pubis. After clamping the drainage tube of the urinary catheter, the bladder was instilled with 50 mL of sterile normal saline injected through a Foley catheter under aseptic condition, the bladder was then emptied by removing the clamp off the drainage tube. IVP was measured using a pressure transducer, and a series of reading were obtained every 4 h apart and their average calculated as one standardized measurement in mmHg (1 mmHg = 1.36 cmH<sub>2</sub>O). Only end-expiratory values were used in an effort to avoid interference from respiratory excursion of the diaphragm into the intra-abdominal space. A sustained increase in IAP was detected based upon at least three consecutive standardized measurements during at least 8 h.

Hemodynamics and other physiologic parameters, including HR, mean arterial pressure (MAP), central venous pressure (CVP), urine output (UO), peak airway pressure (PAP), arterial carbon dioxide partial pressure ( $\text{PaCO}_2$ ), modified respiratory index (MRI) expressed as the arterial oxygen partial pressure ( $\text{PaO}_2$ ) to fraction of inspired oxygen ( $\text{FiO}_2$ ) ratio ( $\text{PaO}_2/\text{FiO}_2$ ), arterial pH, arterial base deficits (BE) and arterial lactic acid, were registered before and after decompression of ACS. The worst Acute Physiology and Chronic Health Evaluation (APACHE) II score and Ranson scoring system during the first 24 or 48 h of SICU stay were recorded respectively in the identification of the severity of pancreatitis. In this study, we applied a Marshall subscore of 2 or more in any of the 6 organs (respiratory, cardiovascular, coagulation, central nervous system, hepatic, and renal) to indicate organ dysfunction associated with IAH (IAP  $> 20$  mmHg), and defined the presence of ACS. MODS was defined as two or more organs having persistently 2 or more Marshall subscores for more than 24 h despite aggressive resuscitation and organ support. Total Marshall scores were computed daily and for the entire duration of the intensive care stay.

All 74 patients with AP were detected using contrast

Table 1 Etiology of attacks in 74 patients with AP

| Etiology of attacks | Number of patients (%) | IAH group No. (%) | Normal IAP group No. (%) |
|---------------------|------------------------|-------------------|--------------------------|
| Gallstones          | 46 (62.16)             | 26(59.09)         | 20 (66.67)               |
| Hyperlipidemia      | 11 (14.86)             | 7 (15.91)         | 4 (13.33)                |
| Alcohol             | 8 (10.81)              | 5 (11.36)         | 3 (10.00)                |
| Idiopathic          | 9 (12.16)              | 6 (13.64)         | 3 (10.00)                |
| Total               | 74                     | 44                | 30                       |

Table 2 Comparison of clinical data on admission between two groups (mean  $\pm$  SD)

| Clinical data on admission | IAP $\geq$ 12 mmHg (n = 44) | IAP < 12 mmHg (n = 30) | $\chi^2$ or <i>t</i> value | <i>P</i> value |
|----------------------------|-----------------------------|------------------------|----------------------------|----------------|
| Age (yr)                   | 62.61 $\pm$ 11.05           | 63.57 $\pm$ 7.71       | -0.41                      | 0.684          |
| Gender (male/female)       | 23/21                       | 16/14                  | 0.01                       | 0.929          |
| APACHE II score            | 16.18 $\pm$ 3.90            | 15.70 $\pm$ 4.25       | 0.50                       | 0.616          |
| Ranson score               | 3.70 $\pm$ 0.93             | 3.47 $\pm$ 0.94        | 1.08                       | 0.285          |
| CTSI                       | 5.25 $\pm$ 2.27             | 5.63 $\pm$ 2.01        | 0.75                       | 0.458          |

APACHE II score: Acute physiology and chronic health evaluation II score; CTSI: CT scan severity index.

enhanced computed tomography (CT) on admission. The contrast-enhanced CT scan severity index (CT-SI) developed by Balthazar and coworkers was used for evaluating severity of pancreatitis<sup>[8]</sup>. CT-SI was measured for all patients on admission in this study. The incidences of pancreatic infection, septic shock, MODS, and the in-hospital mortality were also recorded. Pancreatic infection included infected necrosis and pancreatic abscess. Necrosis formation of the pancreas was assessed by contrast-enhanced CT. Patients with pancreatic necrosis or large peripancreatic fluid collections who manifested clinical signs of sepsis with a non-improving or deteriorating clinical course despite a reasonable time of medical therapy underwent fine-needle aspiration (FNA) of the necrotic areas or fluid collections under CT or ultrasound guidance to determine the presence of bacterial contamination or pancreatic infection.

### Statistical analysis

Patients' clinical records were retrospectively reviewed. Data were analyzed using the software package SPSS version 11.5. Continuous data are presented as mean  $\pm$  SD. Categorical variables are expressed as numbers and percentages for the group from which they were derived. The comparisons of age, gender, APACHE II score and CT-SI on admission, Ranson score within 48 h after admission, incidences of pancreatic infection and MODS, and the in-hospital mortality between the two groups were analyzed using the independent sample *t* test or  $\chi^2$  test as appropriate. Comparison of clinical parameters between before decompression and after decompression of ACS was performed by paired samples *t* test. Bivariate correlations were analyzed by Pearson test between the mean IAP in any 24-h period within the first week after admission and the Marshall score at the same time interval, or, between the IAP on admission and the

APACHE II score on admission or Ranson score within 48 h after admission. Difference was defined as statistically significant if  $P < 0.05$ .  $P^*$  (corrected  $P$ )  $< 0.017$  indicated statistically significant difference in multiple comparisons of complications and outcome between patients with and without ACS in  $\chi^2$  test.

## RESULTS

### IAH group and normal intra-abdominal pressure group

Seventy-four patients (39 men and 35 women) were included in the study; the mean age was 63.00  $\pm$  9.79 years (range, 42-87 years). The mean time interval between onset of AP and admission was 34.97  $\pm$  30.16 h. IAH developed in 44 (59.46%) of 74 patients with AP. The etiologic causes of their AP are detailed in Table 1. The difference in etiologic causes between the two groups was not statistically significant,  $P = 0.803$  (Fisher two-tail exact probability test). The differences in age, gender, APACHE II score, Ranson score and CT-SI on admission were also not statistically significant between IAH group and group with normal IAP (Table 2). Neither age nor gender was correlated with IAH development. Similarly, APACHE II score and CT-SI on admission, and Ranson score within 48 h after admission, contrary to accepted belief, were not found predictive of early IAH development.

During any 24-h period of the first week after admission, the recorded mean IAP was correlated significantly with the Marshall score calculated at the same time interval in IAH group ( $r = 0.635$ ,  $P < 0.001$ ), but IAP on admission had no significant correlation with APACHE II score on admission and Ranson score within 48 h after admission ( $r = 0.127$ ,  $P = 0.248$ , and  $r = 0.145$ ,  $P = 0.263$ , respectively).

### ACS patients

ACS was recorded during the first week after admission in 20 patients (27.03%) in whom IAH (IAP  $>$  20 mmHg) was associated with organ dysfunction or failure. In 14 of these patients, IAH and organ dysfunction were present on admission, 2 patients had IAH on admission and developed organ dysfunction 24-48 h later, whereas 4 patients had respiratory failure on admission without IAH but went on to develop IAH and ACS 3-5 d after admission. Medicine and physical therapy were applied in all IAH patients to promote enterokinesia for recovery of IAH/ACS. The administration of prokinetic motility agents such as erythromycin, metoclopramide, or neostigmine appeared to hold promise in evacuating the intraluminal contents and decreasing the size of the viscera. Moreover, sedation and muscle relaxant (only for mechanical ventilated patients) were also used properly to lower IAP. Seven ACS patients had restoration of organ function with their UBP lowering less than 12 mmHg *via* non-invasive intervention mentioned above. The remaining 13 ACS patients had progressive deterioration of organ function and increases in IAP despite active persistent non-invasive decompression management for 24 h. Therefore, these

**Table 3** Changes in physiological variables after invasive decompressive procedure in patients with ACS ( $n = 13$ , mean  $\pm$  SD)

| Variable                                  | Before decompression | After decompression | $t$ value | $P$ value |
|---|----------------------|---------------------|-----------|-----------|
| MAP (mmHg)                                | 53.77 $\pm$ 8.98     | 74.15 $\pm$ 6.68    | 7.23      | < 0.001   |
| UBP (mmHg)                                | 36.69 $\pm$ 5.33     | 18.31 $\pm$ 3.25    | -8.77     | < 0.001   |
| UO (mL/h)                                 | 21.76 $\pm$ 13.42    | 85.78 $\pm$ 18.46   | 13.29     | < 0.001   |
| CVP (mmHg)                                | 15.01 $\pm$ 5.24     | 13.02 $\pm$ 5.01    | -1.97     | 0.072     |
| BE  | -9.31 $\pm$ 3.09     | -1.69 $\pm$ 2.59    | 6.67      | < 0.001   |
| PH  | 7.28 $\pm$ 0.10      | 7.36 $\pm$ 0.06     | 2.35      | 0.037     |
| PaO <sub>2</sub> /FiO <sub>2</sub> (mmHg) | 129.22 $\pm$ 41.30   | 229.24 $\pm$ 63.47  | 4.33      | 0.001     |
| PAP (cmH <sub>2</sub> O)                  | 41.23 $\pm$ 12.90    | 24.46 $\pm$ 5.41    | -4.25     | 0.001     |
| HR (bpm)                                  | 132.38 $\pm$ 13.68   | 111.62 $\pm$ 12.85  | -5.19     | < 0.001   |
| PaCO <sub>2</sub> (mmHg)                  | 47.61 $\pm$ 11.24    | 38.63 $\pm$ 5.78    | -2.38     | 0.034     |
| Lactate (mmol/L)                          | 4.48 $\pm$ 0.95      | 2.02 $\pm$ 0.80     | -8.11     | < 0.001   |

MAP: Mean arterial pressure; UBP: Urinary bladder pressure; UO: Urine output; CVP: Central venous pressure; BE: Arterial base deficits; pH: Arterial Ph; PaO<sub>2</sub>/FiO<sub>2</sub> (MRI): Arterial oxygen partial pressure/fraction of inspired oxygen; PAP: Peak airway pressure; HR: Heart rate; PaCO<sub>2</sub>: Arterial carbon dioxide partial pressure; Lactate: Arterial lactic acid.

patients had abdominal decompression procedure very soon. The mean time interval between diagnosis of ACS and initiation of invasive decompressive procedure was 28.38  $\pm$  2.29 h (range, 26-33 h). Prior to invasive decompression, aggressive attempts should be made to correct coagulation deficits, acidosis and hypovolemia.

The invasive decompressive procedure included two ways: abdominal percutaneous decompression drainage and decompressive laparotomy with temporary closure. IAP was reduced in one of the two ways. The insertion of abdominal drains was performed in 8 patients under CT or ultrasound guidance in the presence of large intra-abdominal collections more than 800 mL. These patients had their abdomens decompressed by percutaneous placement of a large-bore hemodialysis catheter into the intra-abdominal space, with drainage of intra-abdominal fluid. Percutaneous drainage was a continual process with fluid draining for several days. Once the drainage stopped, the catheter was removed. No complication related to the procedure occurred in our study. Decompressive drainage reduced the IAP by less than 20 mmHg and then further resulted in relief of the IAH in 5 patients. Decompressive laparotomy was performed in the remaining 5 patients with ACS and 3 patients of failure in previous percutaneous abdominal decompressive drainage for the reduction in IAP. The typical open abdomen operation was performed with a temporary silastic covering obtained from the sterilized inner surface of an intravenous bag sewn to the fascia to protect the underlying abdominal contents from injury and desiccation, and to prevent excessive amounts of fluid from leaking onto surrounding bandages. Removal of silastic covering and scheduled closure of abdominal wall should be subsequently attempted as soon as possible after the acute episode resolved and the edema and/or inflammatory fluid collections reduced significantly. No complication directly related to decompressive laparotomy itself occurred in our study.

All patients with bladder pressure of more than

20 mmHg immediately benefited from the alternative of invasive decompression methods. Emergency invasive decompressive procedure resulted in statistically significant improvement in physiologic parameters, with the exception of the CVP, within 24 h after decompression (Table 3). Pre-decompression bladder pressure was significantly elevated, with a mean pressure of 36.69  $\pm$  5.33 mmHg. Abdominal compartment release resulted in a dramatic decrease of IAP to 18.31  $\pm$  3.25 mmHg ( $P < 0.001$ ). The high PAP improved significantly from 41.23  $\pm$  12.90 cmH<sub>2</sub>O pre-decompression to 24.46  $\pm$  5.41 cmH<sub>2</sub>O post-decompression ( $P = 0.001$ ). Other general physiologic condition also improved significantly with decompression, as evidenced by a significant improvement in serum pH, BE, PaO<sub>2</sub>/PaCO<sub>2</sub>, arterial lactic acid, MAP and UO. Only one parameter registered in this study, e.g. CVP, was not affected by decompression for ACS ( $P = 0.072$ ).

### Prognosis

Seventeen of 74 patients died with a mortality rate of 22.97%. It appeared that the incidences of pancreatic infection and MODS in patients with ACS in early stage were considerably higher than other patients without ACS. Subsequently, the unacceptably high mortality rate in patients with ACS during their first week after admission was much higher than that in patients without ACS in the course of their attack of AP (75% *vs* 3.33% and 4.17%) (Table 4).

Multiple comparisons of complications and outcome were made between ACS patients (IAP > 20 mmHg), IAH patients without ACS (12 mmHg  $\leq$  IAP  $\leq$  20 mmHg) and normal IAP patients (IAP < 12 mmHg). The incidences of pancreatic infection, septic shock, MODS and in-hospital mortality in patients with ACS were significantly higher than those in IAH patients without ACS and normal IAP patients, respectively (pancreatic infection:  $\chi^2 = 13.42$ ,  $P < 0.001$ ;  $\chi^2 = 16.93$ ,  $P < 0.001$ , septic shock:  $\chi^2 = 12.84$ ,  $P < 0.001$ ;  $\chi^2 = 22.12$ ,  $P < 0.001$ , MODS:  $\chi^2 = 11.01$ ,  $P = 0.001$ ;  $\chi^2 = 21.33$ ,  $P < 0.001$ , in-hospital mortality:  $\chi^2 = 23.65$ ,  $P < 0.001$ ;  $\chi^2 = 28.32$ ,  $P < 0.001$ , respectively). However, the difference in incidences of pancreatic infection, septic shock, MODS and in-hospital mortality was not statistically significant between IAH patients without ACS and normal IAP patients (pancreatic infection:  $P = 1.000$ , Fisher two-tail exact probability test; septic shock:  $\chi^2 = 0.527$ ,  $P = 0.468$ ; MODS:  $\chi^2 = 2.078$ ,  $P = 0.149$ ; in-hospital mortality:  $P = 1.000$ , Fisher two-tail exact probability test).

### DISCUSSION

The ACS is an increasingly recognized complication of both medical and surgical patients. This syndrome has been described in a wide variety of clinical scenarios and results from a persistent elevation in IAP characterized by graded organ system dysfunction. The definitions and diagnosis of IAH or ACS depend greatly on the accuracy and reproducibility of the IAP measurement technique. As a result, IAP must be measured with an

Table 4 Comparison of complications and outcome between patients with and without ACS

| Complications and outcome | ACS<br>( <i>n</i> = 20)<br>(IAP > 20 mmHg) | IAH ( <i>n</i> = 24)<br>(12 mmHg ≤ IAP<br>≤ 20 mmHg) | Normal IAP<br>( <i>n</i> = 30) (IAP<br>< 12 mmHg) | $\chi^2$<br>value | <i>P</i><br>value |
|---------------------------|--|--|---|-------------------|-------------------|
| Pancreatic infection (%)  | 12 (60.00)                                 | 2 (8.33)   | 2 (6.67)  | 23.84             | < 0.001           |
| Septic shock (%)          | 14 (70.00)                                 | 4 (16.67)  | 2 (6.67)  | 26.34             | < 0.001           |
| MODS (%)                  | 18 (90.00)                                 | 10 (41.67)   | 7 (23.33)   | 21.85             | < 0.001           |
| In-hospital mortality (%) | 15 (75.00)                                 | 1 (4.17)   | 1 (3.33)  | 41.93             | < 0.001           |

MODS: Multiple organ dysfunction syndrome.

accurate, reproducible, and reliable tool. The diagnosis of ACS requires a high level of clinical suspicion combined with an increased IAP, usually obtained *via* UBP measurement. UBP measurement as an estimation of IAP is simple, reliable and widely accepted.

The bladder gold standard measurement techniques reported are not uniform<sup>[9]</sup>. The volume instilled in the bladder is important. This was shown by Fusco *et al*<sup>[7]</sup>, who compared direct laparoscopic insufflation pressure with IVP measured with different bladder volumes. They found that a bladder volume of 50 mL revealed the least bias in measuring elevated IAP. The current standard of IAP measurement in our study *via* the urinary catheter is labor intensive, and its intermittent nature could prevent timely recognition of significant changes in IAP. The continuous IAP measurement proposed by Balogh *et al*<sup>[10]</sup> can be accurately measured via the irrigation port of a three-way catheter and has good agreement with the standard intermittent IAP. Recently, a fully automated IAP measurement technique was described that it can minimize the pitfalls that may alter the accuracy and reproducibility of intermittent IAP measurements (such as volume instilled, zero reference level, air bubbles, over- or underdamping). The IAP catheter is introduced like a nasogastric tube and is equipped with an air pouch at the tip. Automated IAP measurement had good correlation with the standard IVP method<sup>[11]</sup>. Schachtrupp *et al*<sup>[12]</sup> compared different direct and indirect IAP measurement methods in a porcine model and found a very good correlation between the above-mentioned air pouch system and direct insufflator pressure. However, the air pouch system was not available for use in our study.

IAH was defined in our study as a mean IAP  $\geq$  12 mmHg, whereas ACS was defined as a gradually and consistently increased IAP value of > 20 mmHg associated with at least one organ dysfunction or failure that was not previously present. This study confirms that IAH and ACS are frequent occurrences in patients with AP because these conditions were observed in 59.46% and 27.03% of the studied patients, respectively.

Although ideally the diagnosis of ACS should be made based on the clinical picture and confirmed by measurements of bladder pressure or equivalent, Pickhardt and others<sup>[13]</sup> described the CT findings in four patients with confirmed ACS. They reported that the anteroposterior to transverse abdominal ratio was increased (round belly sign) in patients with ACS. The ACS patients had a ratio of 0.85 compared with 0.70 in controls. Al-Bahrani *et al*<sup>[14]</sup> concluded in their

prospective evaluation of CT features that the presence of round belly sign and bowel wall thickening with enhancement on CT images should alert clinicians to the possibility of presence of IAH and ACS, and to prompt measurement of the IAP and consideration of suitable interventions. The radiological data of CT scans that paralleled with the development of ACS in any course of the disease were deficient in our clinical information, so, we could not analyze the CT findings in ACS patients with SAP in our study.

Patients with AP are at risk for IAH/ACS because of the large volume of intra-abdominal and peripancreatic inflammatory fluid collection, capillary leakage caused by increased permeability, bowel and splanchnic edema, resuscitation fluid, and other factors. Gastrointestinal ileus or distension is a common risk factor for IAH among patients with AP. Both air and fluid within the hollow viscera can raise IAP and lead to IAH. IAH also leads to intestinal edema and visceral swelling triggering a vicious cycle. IAH impairs organ perfusion and leads to organ dysfunction. Manifestations of ACS include cardiovascular, pulmonary, renal, splanchnic and neurologic impairment. Hypoperfusion of the gastrointestinal tract was reported at IAP of 12 mmHg<sup>[15]</sup>. Oliguria and marked reduction in cardiac output have been shown to develop at an IAP greater than 20 mmHg<sup>[16,17]</sup>. The relationship among rise in IAP, greater organ dysfunction and, subsequently, higher disease mortality was well illustrated in our study. A positive significant correlation was observed between IAP and Marshall organ dysfunction score. We also observed significant improvement in Marshall score and MODS of patients with resolution of IAH. The overall mortality rate in our study of approximately 23% is comparable to the 10%-50% reported in AP patients by others<sup>[18-21]</sup>. The mortality in ACS patients in our study (75%), however, was much higher than that in patients without ACS which is not acceptable for us, although post-injury ACS has been consistently reported to have a high mortality ranging from 25%-75%. We then compared the early onset of organ dysfunction (within 7 d of admission with AP) and risk of the disease.

While non-operative medical management strategies are now recognized as playing a vital role in both the prevention and treatment of physiologic compromise and organ dysfunction due to elevated IAP, surgical decompression is commonly considered the only treatment for aggravated ACS. All patients with IAH/ACS in our study were initially managed with

noninvasive measures. In an attempt to decrease the elevated IAP, nasogastric decompression, prokinetic motility agents, bowel care, sedation, analgesia and pharmacologic paralysis were administered. Those patients who failed to improve rapidly after institution of these conservative measures underwent percutaneous abdominal decompressive drainage or operative abdominal compartment release. Although the obvious amelioration in physiological variables within 24 h after decompression have been observed in ACS patients, the clinical relevance of ACS in patients with AP in our study was illustrated, in part, by the greater probability of pancreatic infection, MODS and mortality. For this reason, a high index of suspicion and low threshold for decompressive procedure appear appropriate in patients with AP. Patients at risk for ACS warrant close monitoring and we recommend prompt abdominal decompression following documentation of increased IAP in the setting of physiologic compromise, despite in the absence of organ dysfunction/failure.

However, there is no clear consensus on the critical level of IAP at which decompression is necessary. The critical level of IAP requiring decompression thus has not been established for AP patients. Evidence of significant organ dysfunction has been demonstrated at an IAP of 10 mmHg<sup>[22]</sup>. It partially explains why the outcome of ACS patients in our study is poor even though invasive decompression appeared to be effective in reducing IAP and potentially ameliorating IAH-induced physiologic compromise. One of the most important determinants of mortality is the time interval between occurrence of IAH and sustained reduction in IAP of < 12 mmHg by decompression. As shown above, hypoperfusion and acidosis start occurring at pressures from 10 to 12 mmHg, an IAP near 10 mmHg is thus gaining acceptance as a cut-off value in our institution.

Some papers have demonstrated that a persistent splanchnic hypoperfusion may induce irreversible damage in organ function and death<sup>[23-25]</sup>. We speculate that a global mechanism of ischemia and reperfusion may explain these findings. Increased IAP resulted in a decrease of mucosal blood flow to 63% of baseline despite maintaining normal mean arterial blood pressure<sup>[17]</sup>. In addition, elevated IAP could significantly reduce bowel tissue oxygenation due to bowel ischemia<sup>[26]</sup>. In the 1990s, several authors observed a positive correlation between bacterial translocation and IAP in animal models, even when IAP was raised for less than 1 h. This result was caused by increased gut permeability induced by splanchnic ischemia with and without reperfusion<sup>[27,28]</sup>. The mechanism by which the necrotic pancreas becomes infected is unclear, but experimental and clinical data suggest that the gastrointestinal tract is the likely source of organisms, since intestinal colonization by pathogens often precedes pancreatic infection<sup>[29-33]</sup>. The gut clearly plays a major role in the development of MODS. IAH has been shown to be associated with increased bacterial translocation to pancreas and probability of pancreatic infection followed by MODS and death. This increase may be more pronounced when the rise in IAP is followed

by splanchnic ischemia/reperfusion after decompression because of ACS. Moreover, ACS decompression showed to provoke and amplify proinflammatory cytokine release that served as a second insult for the induction of severe organ dysfunction in the two-hit model of MODS<sup>[34]</sup>. Time interval effect of decompression is consistent with the "vulnerable window" of inflammatory mediators cascade priming. As a result, abdominal decompression of established ACS probably causes a fulminant reperfusion syndrome. The mean time interval between diagnosis of ACS and initiation of invasive decompressive procedure in our study was  $28.38 \pm 2.29$  h. The relatively long time for persistence of ACS before invasive decompression might be enough to induce the higher pre-decompression IAP ( $36.69 \pm 5.33$  mmHg) and occurrence of splanchnic ischemia/reperfusion, and soon thereafter, to trigger the bacteria residing within the gastrointestinal lumen to cross the intact intestine into pancreas<sup>[35]</sup>. The sequential effects might mainly contribute to pancreatic infection, MODS and the higher mortality of ACS patients in our study. We therefore advocate performing invasive decompression for an acute IAP of 20-25 mmHg rather than 30-40 mmHg. We also should keep firmly in mind that the earlier treatment is instituted, the more likely a progression to irreversible damage is prevented. The key to managing IAH and ACS is the early recognition of the harmful effects. It is better to prevent ACS than to allow it to occur, and manage the sequelae. However, the timing, indications and threshold value for surgical decompression are controversial with very few large trials available to give firm guidance. Decompression must be strongly considered if the IAP continues to rise or if clinical deterioration occurs. We agree with the concept that IAH is a part of a continuum leading to ACS; therefore, early detection and treatment are preferable to treating the overt clinical manifestations of ACS.

The widely disparate patient populations who may develop IAH/ACS make a standardized therapeutic approach to this syndrome difficult. Thus a single threshold value of IAP cannot be globally applied to the decision making of all patients. No one management strategy can be uniformly applied to every patient with IAH/ACS. Several fundamental management concepts, however, remain appropriate among all patients with AP. While initial conservative measures are implemented and the patient nonetheless proceeds to develop IAPs by greater than 20 mmHg, invasive abdominal decompression should be performed immediately, particularly in the presence of general trend of signs towards overt ACS, including a tendency towards high airway pressures or oliguria refractory to aggressive resuscitation. In AP patients, decompression can be accomplished either by percutaneous decompression with a large-bore catheter inserted or by formal laparotomy. Failure of catheter decompression invariably leads to formal laparotomy. With an increased awareness of the signs of ACS, early conservative treatment of IAH and rapid abdominal decompression when the trend towards the syndrome manifests, clinicians can expect a lower mortality in severe AP patients. In our experience with 74 patients with AP,

the following clinical features may predispose ACS in early stage of the disease: gastrointestinal ileus or distension, a large volume of intra-abdominal and peripancreatic inflammatory fluid collection, massive fluid resuscitation and oliguria.

Indeed, the data presented from our retrospective study raise more questions than answers. Further prospective multi-center studies involving a large number of AP patients are necessary to identify subgroups that might benefit from a therapeutic intervention. The outcome of ACS remains very poor in present study. This result suggests that efforts at prevention may be as fruitful as the efforts directed at early recognition and decompression. Further efforts should focus on prevention of the syndrome. For better prevention of ACS, further studies are essential to identify the independent risk factors for ACS in AP patients and build prediction models for the syndrome to identify high-risk patients with early signs and symptoms of ACS, so as to permit prevention or timely modified treatment before organ failure occurs.

In summary, we conclude that ACS is one of the most important causes of significant morbidity and mortality in AP patients. Early detection and rapid treatment of IAH via abdominal decompression should be essential to preventing the subsequent development of pressure induced organ dysfunction in AP patients.

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## COMMENTS

### Background

Intra-abdominal hypertension (IAH) contributes to organ failure in patients with abdominal trauma and sepsis and leads to the development of abdominal compartment syndrome (ACS). ACS has also been described in patients with severe acute pancreatitis (SAP). Significant visceral edema associated with massive fluid resuscitation, paralytic ileus and formation of pancreatic ascites in patients with SAP can lead to ACS which may cause the early development of multiple organ dysfunction syndrome (MODS), especially in the early stages of the disease. Despite recent advances in the management of patients, SAP remains a disease with an unpredictable clinical course and significant morbidity and mortality. Pancreatic infection and the presence of organ dysfunction still remain the most feared complications and are increasingly recognized as important risk factors for mortality in patients with SAP. The development of ACS in patients with SAP seems to be associated with increased mortality. The clinical impact of IAH/ACS on pancreatic infection and organ failure in SAP patients is needed to investigate.

### Research frontiers

Only recently has the important role of ACS been recognized as a contributing factor for the multiple organ failure commonly seen in SAP. Percutaneous drainage of ascites and surgical decompression are the preferred methods of treatment for ACS. However, some studies, including this study, show that although decompression has a significant effect in lowering IAP, mortality still remains high in SAP patients with ACS. The poor response might be due to an intervention performed too late. Although the 2004 international ACS conference consensus definitions committee has proposed the evidence-based treatment guidelines to assist clinicians in the management of IAH and ACS, there is no clear consensus on the critical level of IAP at which decompression

is necessary. The critical level of IAP requiring decompression thus has not been established for AP patients. Because of the close correlation between ACS and death in SAP patients as suggested by this study, there is a great need for well-designed, prospective clinical trials to clarify the questions and issues that remain unanswered with respect to IAH and ACS.

### Innovations and breakthroughs

The notion that patients with SAP may develop ACS, which necessitates emergency abdominal decompression, has been ignored by some current literatures. The currently prevailing paradigm calls for non-operative management of SAP as long as there is no evidence of infection. The authors of this study proposed that there is a subset of patients who may necessitate an emergency abdominal decompression or laparotomy in the absence of infection in order to decompress a clinically significant ACS, which is associated with the acute pancreatitis (AP).

### Applications

The present study implicated that the timing of surgical decompression may play a crucial role in improving poor survival rates of SAP patients with ACS. Increased awareness of the syndrome of IAH/ACS in AP and transvesical measurement of intra-abdominal pressure (IAP) will reveal its prevalence and significance. This experience with the 74 patients may reinforce the enthusiasm for prevention of ACS and decompression in SAP patients with IAH. This study also gave proof of necessity for establishing a critical IAP level at which abdominal decompression or laparotomy should be performed for SAP patients.

### Terminology

IAP is the steady-state pressure concealed within the abdominal cavity. IAH is a sustained or repeated pathological elevation in IAP  $\geq 12$  mmHg. ACS is a sustained IAP  $> 20$  mmHg associated with new organ dysfunction/failure.

### Peer review

Although the IAP was described by Etienne-Jules Marey in 1863 and ACS described in details by Korn *et al* in 1984 and more information is appearing recently in the literature, it is still important to gather more knowledge about ACS complicating severe pancreatitis. This article constitutes a fairly good number of patients with ACS.

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