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RISK FACTORS FOR INCREASED INTRA-ABDOMINAL PRESSURE IN SEVERE ACUTE PANCREATITIS

Alex. Carâp[1,2], F. Popa[1,2], B. Socea[1,2], C. Moculescu[2], Georgeta Păunică-Panea[2], I. Păun[3], V. Budu[1], V. Constantin[1,2]

[1]*Surgery Department, „Carol Davila" University of Medicine and Pharmacy*
[2]*General Surgery Department, „Sfântul Pantelimon" Emergency Clinical Hospital*
[3]*General Surgery Department, Craiova University of Medicine and Pharmacy, Craiova, Romania*

Summary

Background: Under-diagnosed and untreated abdominal compartment syndrome (ACS) is a potential contributing factor to the development of early organ failure seen in patients with severe acute pancreatitis (SAP). It is estimated that 40% of SAP patients will develop IAH and about 10% will develop ACS requiring surgical decompression. The true incidence, however, is not known, as few centers measure the IAP.
Materials and methods: We analyzed 26 cases of SAP admitted and treated in our department between July 2014 and March 2015. In all cases IAP was monitored as per the instructions of the WSACS every 8 hours. In patients diagnosed with IAH or ACS the risk factors proposed by the WSACS were assessed for frequency. Relations between the development of IAH/ACS and the values recorded on the Modified Marshall Scoring system and the SOFA scores were investigated.
Results: The risk factors that proved to have a strong association with the development of IAH/ACS were multiple organ failure on SAP diagnosis, obesity, positive fluid balance, and total SOFA score on SAP diagnosis.
Discussion: Research in the fields of SAP and ACS is ongoing. Identifying risk factors for the development of ACS in SAP patients can improve the rates of morbidity and mortality, reduce costs and are essential for the better management of these difficult conditions.
Conclusions: The associations found by our analysis can lead to further research in risk factor identification and prevention of ACS. Multiple organ failure, obesity and a positive fluid balance were found to be associated with increased intra-abdominal pressure or abdominal compartment syndrome more often.
Key words: severe acute pancreatitis, risk factors, abdominal compartment syndrome

Résumé

Facteurs de risque de la pression intra-abdominale accrue dans la pancréatite aiguë sévère

Contexte: Le syndrome du compartiment abdominal non traité et sous-diagnostiquée (ACS), est un facteur contributif potentiel au développement de la défaillance d'un organe, observée chez les patients atteints de pancréatite aiguë sévère (SAP). On estime que 40% des patients avec SAP vont développer IAH et environ 10% développeront ACS nécessitant une décompression chirurgicale. L'incidence réelle, cependant, n'est pas connue, seulement quelques centres mesurant l'IAP.
Matériels et méthodes: Nous avons analysé 26 cas de SAP admis et traité dans notre département entre Juillet 2014 et Mars 2015. Dans tous les cas IAP a été surveillée selon les instructions de la WSACS, toutes les 8 heures. Chez les patients diagnostiqués avec IAH ou ACS, les facteurs de risque proposés par les WSACS ont été évalués concernant la fréquence. Les relations, entre le développement de l'AIH / ACS et les valeurs enregistrées sur le système de notation Marshall Modifié et les scores de SOFA, ont été étudiées.
Résultats: Les facteurs de risque qui se sont avérés avoir une forte association avec le développement de l'AIH / ACS étaient la défaillance multi viscérale sur le diagnostic de début du SAP, l'obésité, l'équilibre hydrique positif et le score total de SOFA dans l'étape du diagnostic de SAP.
Discussion: La recherche dans les domaines de la SAP et ACS est en cours de développment. Identifier les facteurs de risque pour le développement de l'ACS chez les patients avec SAP peut améliorer les taux de morbidité et de mortalité, réduire les coûts, et sont essentiels pour une meilleure gestion de ces conditions difficiles.
Conclusions: Les associations trouvées par notre analyse peuvent conduire davantage à augmenter la recherche pour l'identification des facteurs de risque et la prévention de l'ACS. Défaillance multiviscérale, l'obésité et un équilibre positif de fluide ont été trouvés à être associée à une augmentation de la pression intra – abdominale, ou le syndrome du compartiment abdominal le plus souvent.
Mots clés: pancréatite aiguë sévère, facteurs de risque, syndrome du compartiment abdominal

Correspondence address: *Assistant Professor Alexandru Carâp*
Surgery Department, "St. Pantelimon" Emergency Clinical Hospital, Surgery Department
340-342 Pantelimon Street, District 2, Bucharest, Romania e-mail: alexandru_carap@hotmail.com

Introduction

Under-diagnosed and untreated abdominal compartment syndrome (ACS) is a potential contributing factor to the development of early organ failure seen in patients with severe acute pancreatitis (SAP). Intra-abdominal hypertension and abdominal compartment syndrome are most common among critically ill adults [1]. Both of these conditions have been linked with renal failure [2, 3] multiple system and organ failure [4] and elevated mortality [5, 6].

As clinical examination is inaccurate for detecting raised intra-abdominal pressure (IAP), intra-abdominal hypertension (IAH), and ACS research and management rely upon accurate IAP measurements [7]. The trans-bladder technique, due to its simplicity and low cost is recommended by the World Society of Abdominal Compartment Syndrome (WSACS) [8]. The WSACS recommends protocolized monitoring and management of IAP in order to avoid confounding factors (nurse shifts, body position, zero reference).

Recent advances in the management of SAP (aggressive fluid resuscitation, more accurate indications and timing of surgical intervention, advances in monitoring and management of organ dysfunctions, increased use of enteral nutrition, early sphincterotomy in patients with common bile duct stone-induced pancreatitis) have all contributed to improved survival. Mortality rates have steadily decreased in the last decades from values near 50% to values around 15-20% [9]. Although mortality rates have dropped overall it has been observed that mortality in the first 14 days of the disease has failed to improve [10]. One hypothesis is that a high proportion of deaths in the early phase is caused by unrecognized and untreated ACS that leads to early Multiple System and Organ Failure (MSOF). The development of MSOF is the major predictor of a poor outcome.

It is estimated that 40% of SAP patients will develop IAH and about 10% will develop ACS requiring surgical decompression. The true incidence, however, is not known, as few centers measure the IAP. Recent advents of management can lead us to the conclusion that the prevalence is on the rise as aggressive fluid resuscitation in the early phase of the treatment is ubiquitous and as surgery (i.e. necrosectomy) is delayed as long as possible.

While numerous papers have studied the risk factors for IAH and/or ACS, their interpretation is difficult due to significant heterogeneity, varying patient populations (trauma patients, purely medical conditions, elective and emergent surgery, general surgery procedures or vascular procedures) [11, 12, 13, 14]. The recent risk factors proposed in the latest WSACS guideline were reported to be opinion- or pathophysiology based and occur among nearly all of the patients admitted to the ICU, so identifying evidence based risk factors would lead to a better prevention strategy and management.

SAP is in itself a risk factor for the development of IAH/ACS according to the WSACS guidelines. It is associated with other factors that are listed by the WSACS as risk factors for IAH/ACS development like aggressive fluid resuscitation, visceral edema, fairly frequent intraperitoneal and retroperitoneal fluid. Therefore, the assessment of risk factors for IAH/ACS development in SAP is important.

Materials and Method

We analyzed 26 cases of SAP admitted and treated in our department between July 2014 and March 2015. In all cases IAP was monitored as per the instructions of the WSACS every 8 hours. The method for measurement used was the manometric, Harrahill technique [15]. Data were collected regarding the diagnosis of SAP and IAH and ACS. General epidemiological variables and clinical, imagery and lab results were used for the identification of risk factors for the development of IAH/ACS. Correlations between the Sequential Organ Failure Assessment (SOFA) and the Modified Marshall scoring systems and development of IAH/ACS were investigated.

SAP was defined according to the Acute Pancreatitis Classification Working Group revision of 2012 [16]. Acute pancreatitis was diagnosed on the presence of the following 2 features: a) upper abdominal pain of acute onset often radiating through to the back and b) serum amylase or lipase activity greater than 3 times normal. As not all patients had cross-sectional abdominal imaging this was not considered essential for the diagnosis. SAP was defined as acute pancreatitis with persistent single or multiple organ failure with a duration greater than 48 hours (see Table 1). Organ failure was defined as a value of ≥ 2 on any of the sub scores of the modified Marshall Scoring System (see Table 2). The modified Marshall scoring system has the merit of simplicity, universal applicability across international centers, and the ability to stratify disease severity easily and objectively. All patients diagnosed with SAP were monitored in the ICU (intensive care unit) and all further assessments took place in the ICU.

IAH and ACS were defined according to the WSACS consensus definitions of 2013 [8]. IAH was diagnosed when IAP was higher or equal to 12 mmHg and ACS was diagnosed when the IAP was higher than 20 mmHg and a new organ dysfunction developed (see Table 3). Organ dysfunctions were defined according to the SOFA score classification (see Table 4).

IAP measurements were made using the manometric Harrahill technique (Fig. 1). The technique uses the patient's own urine as a transducing medium. The Foley catheter is

Table 1 - Severity of acute pancreatitis

Mild acute pancreatitis
Lack of organ failure and local/systemic complications
Moderately severe acute pancreatitis
Transient organ failure - organ failure that resolves within 48 hours and/or
Local or systemic complications
Severe acute pancreatitis
Persistent single or multiple organ failure (>48 hours)

Table 2 - Modified Marshall Scoring System

Organ System	Score				
	0	1	2	3	4
Respiratory (PaO_2/FIO_2)	> 400	301-400	201-300	101-200	≤ 101
Renal* (serum creatinine, mg/dl)	< 1.4	1.4-1.8	1.9-3.6	3.6-4.9	> 4.9
Cardiovascular** (systolic blood pressure, mmHg)	> 90	< 90 Responsive to fluid resuscitation	< 90 Not responsive to fluid resuscitation	< 90 pH < 7.3	< 90 pH < 7.2
For non-ventilated patients, the FiO_2 can be estimated from below:					
Supplemental oxygen (l/min)		FiO_2 (%)			
Room air		21			
2		25			
4		30			
6-8		40			
9-10		50			

A score of 2 or more in any system defines the presence of organ failure.
* A score for patients with pre-existing chronic renal failure depends on the extent of further deterioration of baseline renal function. No formal correction exists for a baseline creatinine ≥ 1.4 mg/dl.
** Off inotropic support.

Table 3 - Definitions of IAH and ACS

Intra-abdominal hypertension is graded as follows	
Grade I	IAP 12-15 mmHg
Grade II	IAP 16-20 mmHg
Grade III	IAP 21-25 mmHg
Grade IV	IAP > 25 mmHg
Abdominal Compartment Syndrome	
New organ dysfunction/failure associated with a sustained IAP > 20 mmHg	

IAH - Intra-abdominal hypertension
ACS - Abdominal Compartment Syndrome
IAP - Intra-abdominal pressure

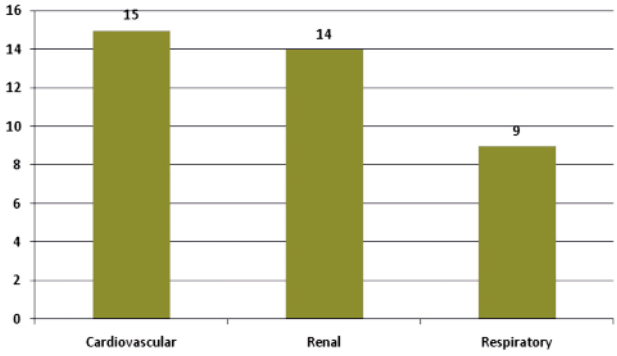

Figure 1 - Organ dysfunctions (as identified with the Modified Marshall Scoring System)

clamped just above the urine collection bag. The tubing is then held in a position of 30 to 40 centimeters above the symphysis pubis and the clamp is released. The IAP is indicated by the height (in cm) of the urine column from the midaxillary line. This estimation of the IAP can only be done for patients that have sufficient urine output. In oliguric patients 50 ml saline were injected as priming. The technique is needle-free and poses no risks for injury. It allows repeated measurements, is very unexpensive and fast with minimal manipulation. This technique has the advantage that it can be performed by any member of the health care team at the bedside. All measurement registered values in cm H20 that were immediately converted to mm Hg. IAP measurements were undertaken every 8 hours, starting with

Table 4 - The Sequential Organ Failure Assessment (SOFA) Score

SOFA score	1	2	3	4
Respiration				
PaO_2/FIO_2 (mmHg)	< 400	< 300	< 220	< 100
SaO_2/FIO_2	221-301	142-220	67-141	< 67
Coagulation				
Platelets x $10^3/mm^3$	< 150	< 100	< 50	< 20
Liver				
Bilirubin (mg/dl)	1.2-1.9	2.0-5.9	6.0-11.9	> 12.0
Cardiovascular*				
Hypotension	MAP < 70	Dopamine ≤ 5 or dobutamine (any)	Dopamine > 5 or norepinephrine ≤ 0.1	Dopamine > 15 or norepinephrine > 0.1
CNS				
Glasgow Coma Scale	13-14	10-12	6-9	< 6
Renal				
Creatinine (mg/dl) or urine output (ml/d)	1.2-1.9	2.0-3.4	3.5-4.9 or < 500	> 5.0 or < 200

MAP, mean arterial pressure; CNS, central nervous system; SaO_2, peripheral arterial oxygen saturation.
* Vasoactive medications administered for at least 1 hr (dopamine and norepinephrine μmg/kg/min)

admission, for every patient diagnosed with SAP.

In patients diagnosed with IAH or ACS the risk factors proposed by the WSACS [8] were assessed for frequency. Relations between the development of IAH/ACS and the values recorded on the Modified Marshall Scoring system and the SOFA scores were investigated.

Results

The study population is made up of 26 patients with a mean age of 54 years. The male to female ratio was 18 to 8. 21 of the patients were from an urban environment and 3 were from the surrounding rural settlements.

Figure 1 shows the organ failures that led to the diagnosis of SAP in the 26 patients studied. Assessment of organ failure was performed using the Modified Marshall Scoring System. 16 patients presented with one organ dysfunction (7 renal, 5 cardiovascular, 4 respiratory), while the remaining 10 presented with multiple organ failure. Cardiovascular failure was identified in 15 patients, renal failure in 14 patients and respiratory failure in 9 patients.

The etiology of the disease was identified in 23 cases, while 3 cases were considered to be idiopathic cases. 17 patients reported chronic alcohol consumption, 4 patients were diagnosed with gallstones, 1 patient had high values of blood lipids and one patient was diagnosed with drug induced pancreatitis (enalapril; the patient had a previous episode of mild AP that was diagnosed as drug induced pancreatitis following enalapril). Figure 2 presents the etiology of the study population.

Of the 26 patients investigated, 13 developed IAH or ACS (2 patients were diagnosed with ACS). We compared common risk factors for the development of IAH and ACS between the two groups of patients. The results are shown in Table 5. Positive fluid balance was defined as a greater than 1000 ml difference between fluid administration and urine output on a 24 hour period. This calculation was made at any point from the diagnosis of SAP until the development of IAH/ACS. Total SOFA score was calculated at the time of diagnosis of SAP and admission in the ICU. Mean ages for the two groups of patients was 51 and 55, respectively. The 13 patients who did not develop IAH/ACS had biliary pancreatitis in 2 cases, reported alcohol consumption in 7 cases, had drug induced pancreatitis in 1 case and idiopathic SAP in one case. The group of patients that developed IAH/ACS during their admission had biliary pancreatitis in 2 cases, alcohol related SAP in 10 cases and hyperlipedimia in one case. At the time of SAP diagnosis 16 patients had one organ failure, 12 of them did not develop IAH/ACS, 4 patients eventually did. Of the 10 patients that presented with two or more organ dysfunctions at the time of SAP diagnosis, one did not develop IAH/ACS while 9 did. Positive fluid balance was identified 2 times in the group that did not develop IAH/ACS and 8 times in the group that did. Contrast enhanced computed tomography was available in 21 patients. More than a 50% pancreatic necrosis was diagnosed in 7 patients that did not develop IAH/ACS and 6 patients that did. Average total SOFA score for the group that did not develop IAH/ACS was 7.3 and 8.2 for the group that did.

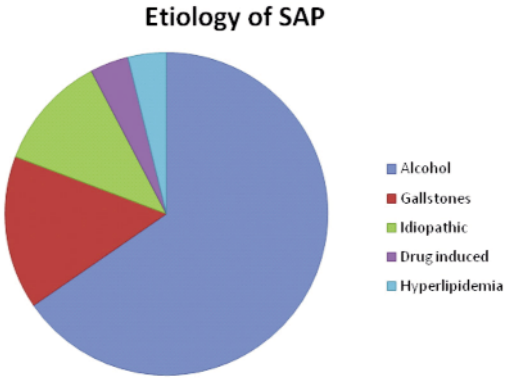

Figure 2 - Etiology of Severe Acute Pancreatitis (SAP)

Overall mortality for the group was 4 patients, 3 patients from the group with IAH and ACS. ACS was treated in one case with decompressive laparotomy and in one case with conservative measures but both resulted in deaths.

Discussion

Intra-abdominal hypertension and abdominal compartment syndrome are relatively rare clinical entities that generally occur in ICU patients. However rare, these entities are coupled with high rates of mortality and morbidity. They are often under diagnosed because of a lack of awareness, and

Table 5 - Risk factors for IAH or ACS

		Did not develop IAH/ACS	Developed IAH/ACS
Age (years, mean)		51	55
Etiology	Biliary	2	2
	Alcohol	7	10
	Other	Drug induced - 1, Idiopathic - 3	Hyperlipidemia - 1
Organ failure (organ/system interested) before IAH/ACS		Single organ failure - 12	
Multiple organ failure - 1		Single organ failure - 4	
Multiple organ failure - 9			
Obesity (BMI > 30 kg/m^2)		4/13	9/13
Positive fluid balance		2/13	8/13
> 50% necrosis on CECT		7/13	6/13
Total SOFA score (average)		7.3	8.2

a lack of a clear understanding of the mechanisms, risk factors and treatment options available. While the open abdomen is quickly gaining ground after damage control surgery in trauma centers, the transition to open abdomen and decompressive laparotomy is slower for non-traumatic entities.

Severe acute pancreatitis is listed as a risk factor for IAH and ACS. Several mechanisms can be attributed to this association. Severe acute pancreatitis is characterized by systemic inflammatory response and large fluid losses in the interstitial space, leading to bowel and abdominal visceral edema. In some instances fluid collections in and around the pancreas can be very large and increase abdominal pressure in themselves. Severe acute pancreatitis is often associated with bowel ileus and its consecutive luminal enlargement. The level of fluid loss in acute pancreatitis is common knowledge and one of the mainstays of therapy is large volume fluid replacement. This, in turn, can lead to generalized edema, including edema of the abdominal content. For all these reasons the WSACS recommends that SAP patients should have their abdominal pressure monitored. A further controversy exists as to what the best treatment for ACS in the setting of SAP is. Surgical intervention should be delayed for as long as possible in SAP for fear of contamination and metabolic failure. Therefore, decompressive laparotomy is a difficult decision to be made for ACS and SAP.

The identification of risk factors for the ACS in patients with SAP could help prevent IAH and ACS in patients with pancreatitis. This would lead to lower morbidity and mortality rates, a further delay in the surgical intervention would be possible and it would probably result in fewer resources being spent.

Conclusions

Our study compared SAP patients and tried to identify certain patterns and risk factors. The comparison between the two groups lacks the statistical power due to the small sample size and retrospective nature. However, the findings can lead to further research and a better understanding of clinical associations between ACS and SAP.

Age was not found to vary significantly between the two groups. The comparison of etiologies revealed no major differences. Multiple organ failure, as defined by the Modified Marshall score, was clearly associated with the development of IAH/ACS more often (9:1). This can be interpreted as a greater severity of the pancreatitis process leading to IAH/ACS and possibly to a greater need for aggressive fluid resuscitation. In our series, obesity was more frequent in the group with IAH/ACS (9:4). Positive fluid balance was identified in 8 patients who developed IAH/ACS versus just 2 in the group that did not. This is one of the major areas of interest when discussing prevention of the ACS. While aggressive fluid resuscitation clearly has its benefits in SAP, its degree is very simple to control and intervene upon. Necrosis of more than half of the pancreas proved to be found in the same proportion in the two groups. SOFA score was higher in the group that developed IAH/ACS related to the already high proportion of multiple organ failure patients or to increased rate of disease progression.

Research in the fields of SAP and ACS is ongoing. Identifying risk factors for the development of ACS in SAP patients can improve the rates of morbidity and mortality, reduce costs and are essential for the better management of these difficult conditions. The associations found by our analysis can lead to further research in risk factor identification and prevention of ACS.

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