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Increased intra-abdominal pressure: is it of any consequence in severe acute pancreatitis?

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Abstract

Background. Increased intra-abdominal pressure (IAP) is detrimental for the recovery of organ function in trauma and emergency patients. The aim of this study was to assess the correlation between the dynamics of IAP and organ dysfunction in severe acute pancreatitis (SAP). *Materials and methods*. Management of SAP between 2000 and 2004 was analysed. SAP was classified according to Atlanta 1992. Organ dysfunction, systemic inflammatory response syndrome (SIRS) and outcomes in relation to the IAP were assessed. IAP was measured indirectly. *Results*. A total of 65 patients, with an average APACHE II score of 6.44, complied with the Atlanta criteria. In all, 34 patients received conservative treatment and 31 were operated. SIRS was observed in 59 cases and multiple organ dysfunction syndrome (MODS) in 61 cases. IAP was significantly higher in the 25 most complicated patients requiring renal replacement therapy (RRT), compared with 40 patients without RRT, 31.72 vs 21.4 cm/H_2O ($p = 0.037$). IAP interrelated positively with SOFA score ($r = +0.371$, $p < 0.01$) and organs involved ($r = +0.356$, $p < 0.01$), and negatively with platelet count and enterally provided volume ($r = -0.284$, $p < 0.01$; $r = -0.5$, $p < 0.01$, respectively). Overall mortality (9.2%) was associated with surgery and sustained increase of the IAP over 25 cm/H_2O. Our data support the pathophysiological interrelation of elevated IAP and development of organ dysfunction. *Conclusion*. Development of organ dysfunction in SAP could be associated with increased IAP. Grade III increase of IAP should be considered as an indicator for revision of treatment modalities.

Key Words: *Severe acute pancreatitis, intra-abdominal pressure, organ dysfunction*

Introduction

Despite recent evidence-based experience in the management of severe acute pancreatitis (SAP) it is too early to say that this disease could be taken under control. The mortality rate is considerably high even in the centres of excellence, reaching up to 15–25% [1–3]. Early risk factor assessment is one of the main determinants for the appropriate management of the disease. Different severity assessment scoring systems and single parameters have been introduced for this purpose such as the APACHE II score, Ranson criteria, Imrie score, Balthasar score, and others [4,5]. Clinical utility of these systems is mainly of prognostic value and gives us the possibility of following a certain treatment strategy. However, a more dynamic assessment of the early signs of deterioration of the clinical course is crucial for further improvement of treatment results in the most severe category of patients. One of the main dynamic pathophysiological events in the early course of SAP is systemic inflammatory response syndrome (SIRS) as a result of proinflammatory cytokine effects, with the characteristic changes in vascular permeability [6]. However, diagnostic efficacy of the cytokine detection is not clinically approved [7]. A more practical approach could be assessment of the initial signs of organ dysfunction according to MODS (multiple organ dysfunction syndrome) or SOFA score. These scores are mainly applicable in an intensive care unit (ICU) setting because of the necessity of multi-parameter data collection. At the same time, markedly increased intra-abdominal pressure (IAP) is recognized as a detrimental factor for the recovery of organ function in trauma and abdominal emergency patients [8]. Negative physiological sequel of markedly increased IAP is recognized as a crucial factor in the development of MODS; however, it is mainly mentioned in association with trauma patients. Measurement of the IAP is reported as a clinical routine for detection of acute abdominal compartment syndrome and recognition of those patients for whom emergency laparotomy is indicated when conservative ICU treatment fails to reduce IAP [9]. Although it is noted that acute pancreatitis is a disease commonly associated with increased IAP, no data are available regarding the clinical utility of the routine measurement of IAP in patients with SAP. The aim of

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this study was to assess whether increased IAP affects the clinical course and reflects on the effectiveness of conservative treatment, as well as to investigate the correlation between the degree of organ dysfunction and dynamics of IAP in patients suffering SAP.

Materials and methods

Our experience in the management of SAP between the years 2000 and 2004 was analysed retrospectively. SAP was classified according to Atlanta 1992 [10]. All patients were treated in an ICU. The dynamics of organ dysfunction, clinical course of SIRS, main physiological parameters and outcomes in relation to the IAP were assessed. IAP measurement was done indirectly through the urinary bladder [11]. Only patients with repeated IAP measurements were included.

Diagnosis of SAP was supported by evidence of severe clinical presentation of the disease, threefold increase of the lipase activity in blood and one of the following criteria: SIRS and/or signs of organ dysfunction, APACHE II score ≥ 6. Necrotizing pancreatitis was diagnosed when ultrasound and CT scan or intraoperative findings demonstrated evidence of necrotic areas in the pancreatic gland or peripancreatic area; CRP was ≥ 150 mg/L.

Organ failure was defined according to the recommendations of the Consensus Conference of the American College of Chest Physicians/Society of Critical Care Medicine in 1991 [12,13]. Accordingly, SIRS was diagnosed if two or more of the following conditions were detected: (a) temperature above 38°C or below 36°C, (b) heart rate above 90 beats/min, (c) respiratory rate above 20 breaths/min or arterial carbon dioxide tension below 32 mmHg, and (d) white blood cell count above 12 000/mm^3 or below 4000/mm^3, or immature (band) forms accounting for more than 10% of neutrophils present [14]. A MODS was diagnosed if dysfunction of more than one organ was detected, requiring intervention to maintain homeostasis. SOFA score was calculated for daily assessment of the dynamics of organ dysfunction. Radiological evidence of basal atelectasis, pneumonia or pleural effusion was recorded separately from the pulmonary dysfunction assessed by SOFA score and classified as pulmonary complications. Acidosis was diagnosed when the pH in the peripheral blood was <7.2. All patients were retrospectively stratified in two groups for better assessment of the physiological role of increased IAP on the clinical course of the disease. The landmark for stratification was IAP ≥ 25 cm/H_2O, correspondent value of the abdominal compartment grade III–IV.

Hospital and ICU stay, complication rate and main outcomes were analysed. Statistical comparison was done with paired samples t test. All clinical data were expressed as average $\pm$ standard deviation (SD). Correlation data were calculated using Pearson's and Spearman's correlation test. The data analysis was performed with SPSS software version 8.0 (SPSS Inc.).

Results

In total 65 patients with average age of 47.87 ± 14.43 matched the inclusion criteria. Of these patients, 45 were male and 20 were female patients, admitted on average 2.3 days from the onset of the disease. APACHE II score was 6.44 ± 4.7 on admission for the whole group. All patients received initial conservative treatments including organ support, active recovery of the tissue perfusion and reduction of the fluid sequestration in the third space by means of isovolaemic haemodilution with adequate colloid/crystalloid infusions. The main indications for the application of the renal replacement therapy were deterioration of the clinical course mainly due to progression of organ dysfunction and critical increase of the IAP after the initial 24–48 hours of therapy. Blood purification therapy included haemodialysis and/or continuous veno-venous haemofiltration (CVVH). Conservative treatment alone was successful in 34 patients. The main indication for surgical intervention was infection. Progressive deterioration of the clinical course despite initial conservative treatment or obscure diagnosis at admission, in some cases, was the specific indication for surgery. Laparotomies with sequestrectomy, mobilization of the peripancreatic region including liver and splenic flexure of the colon and insertion of the lavage system usually were performed. Abdominal closure in the majority of cases was semi-open. Additional surgical interventions were needed in 31 cases.

The clinical course was complicated by development of SIRS in 59 patients and development of MODS in 61 patients. Increase of the IAP below the level of 25 cm/H_2O reaching on average 17.24 ± 3.94 cm/H_2O complicated the clinical course in 41 cases. However, in 24 patients, IAP exceeded 25 cm/H_2O, reaching 39.25 ± 14.67 cm/H_2O for this group. Comparison with the t test did not reveal any significant difference in the results of the incidence of the organ dysfunction according to SOFA score calculation when comparing patients who did not reach elevation of the IAP up to 25 cm/H_2O and those who did reach >25 cm/H_2O, except in the higher rate of pulmonary dysfunction in the more hypertensive group. At the same time, there were six lethal outcomes associated with abdominal compartment grade III–IV compared with zero deaths in those who did not reach elevation of the IAP up to 25 cm/H_2O, $p = 0.011$ (Table I).

The profile of the IAP was significantly higher in the 25 most complicated patients who required renal replacement therapy (RRT), compared with 40 patients who were managed without RRT, 31.72

Table I. Development of SIRS, MODS, complication rate and mortality in patients with IAP <25 cm/H_2O and >25 cm/H_2O.

Parameter	IAP <25 cm/H_2O ($n=41$)	IAP >25 cm/H_2O ($n=24$)	p value
SIRS	36	23	NS
MODS	38	23	NS
Renal dysfunction	10	12	NS
Encephalopathy	2	5	NS
Haematologic dysfunction	20	17	NS
Pulmonary dysfunction	13	14	0.008
Atelectasis	1	5	NS
Pneumonia	4	7	NS
Pleural effusion	13	9	NS
Metabolic acidosis	2	5	NS
Exitus	0	6	0.011

IAP, intra-abdominal pressure; MODS, multiple organ dysfunction syndrome; SIRS, systemic inflammatory response syndrome.

(12–70) vs 21.4 (10–78) cm/H_2O, $p=0.037$, respectively (Figure 1).

Correlation test for all available measurements of the IAP and corresponding values of the SOFA score demonstrated positive interrelation, $r=+0.371$, $p<0.01$ (Figure 2). The same tendency was noted with IAP and the number of organs involved, $r=+0.356$, $p<0.01$. Again, the frequency of cases of liver, renal and pulmonary dysfunction positively correlated with IAP, accordingly $r=+0.305$, $p<0.01$; $r=+0.167$, $p<0.01$; $r=+0.153$, $p<0.05$, respectively. Negative interrelation was observed with platelet count and enterally provided volume, $r=-0.284$, $p<0.01$; $r=-0.5$, $p<0.01$, respectively.

There was no statistical difference when comparing the degree of the IAP among operated and conservatively treated patients (Table II, Figure 3) and, according to medical records, elevation of the IAP was not considered to be the single indication for surgery. In contrast, we observed a significantly higher incidence of organ dysfunction and complication rate in patients who underwent surgical intervention

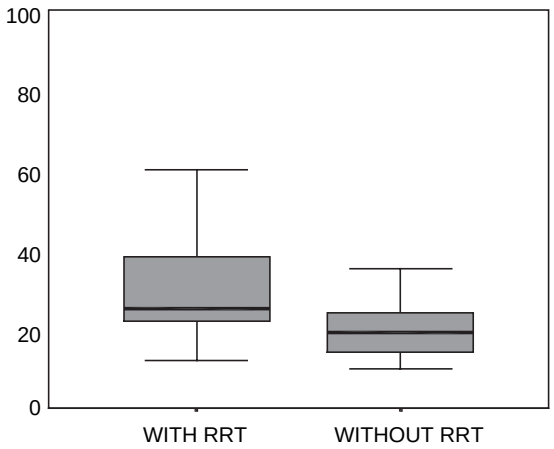

Figure 1. Profile of the intra-abdominal pressure (IAP) in patients who were treated with or without renal replacement therapy (RRT).

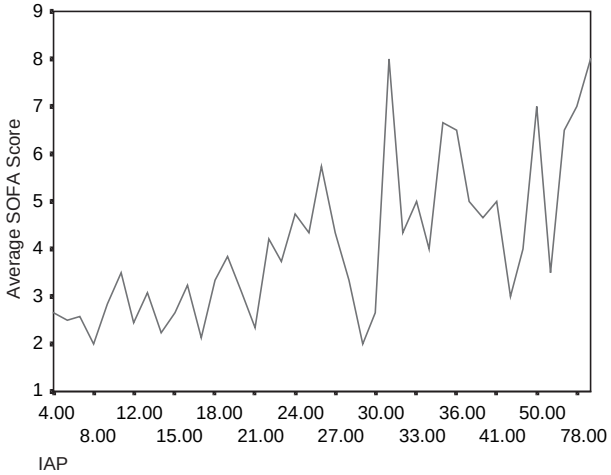

Figure 2. Positive interrelation with intra-abdominal pressure (IAP) and SOFA score.

compared with conservatively treated patients. Predominant incidence of pulmonary complications and pulmonary dysfunction was evidently associated with renal dysfunction and development of abdominal compartment grade III–IV either before or after surgical intervention (Table III). The average time for surgical intervention in our series was 6.87 ± 10.48 days after admission. Unfortunately the average timing of surgical intervention was affected by a certain number of patients who were operated early in the course of SAP. Generally we have followed the strategy of postponing surgical intervention as much as possible after the third week. However in some cases other colleagues ignored this strategy. It is noteworthy that the dynamics of the IAP were not considerably affected by surgical intervention and that most complications developed after surgical intervention (Table IV). Significantly longer ICU stay and hospital stay in operated patients partially reflected advantages of conservative strategy and disadvantages of early surgical intervention.

The overall mortality rate in the analysed group of patients reached 9.2% (six cases). All lethal outcomes were associated with sustained increase of the IAP over 25 cm/H_2O (an average 40.17 ± 16.5 cm/H_2O) corresponding to abdominal compartment grade III–IV and early surgical intervention. The clinical

Table II. Clinical course in operated/non-operated patients.

Parameter	Operated	Not operated	p value
Number	31	34	–
Mean IAP (cm/H_2O)	27.67	23.26	NS
APACHE II (points)	7.16	5.79	NS
SIRS (no. of cases)	29	30	NS
MODS (no. of cases)	29	32	NS
Hospital stay (days)	45.32	18.23	<0.05
ICU stay (days)	16.6	7.9	0.01

IAP, intra-abdominal pressure; ICU, intensive care unit; MODS, multiple organ dysfunction syndrome; SIRS, systemic inflammatory response syndrome.

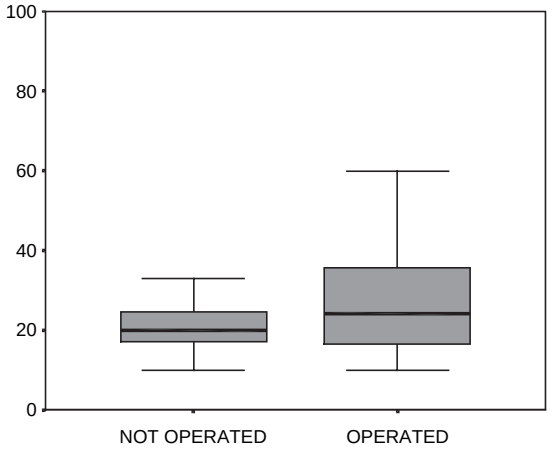

Figure 3. Profile of the intra-abdominal pressure (IAP) in operated and non-operated patients.

course of patients with lethal outcomes was associated with a high incidence of postoperative complications (Table V).

Discussion

Negative clinical consequences of the sustained increase of the IAP are well established mainly in trauma patients, and a certain degree of the abdominal compartment is considered a strong indication for abdominal exploration [15,16]. However, the real pathophysiological role of the abdominal compartment syndrome, which can develop due to marked increase of the IAP in patients with SAP, is not clearly defined. Our retrospective study aimed to clarify whether there is a correlation between elevation of the IAP, the clinical course of the disease and the mode of treatment in this category of patients. The possibility of such an important clinical physiological connection was based on evidence that disturbances of the microcirculation and insufficient perfusion/oxygenation of the end organ is claimed to be the central pathophysiological event in the sepsis-like

Table III. Complication rates* in operated/non-operated patient groups.

Complication	Operated ($n=31$)	Not operated ($n=34$)	p value
Renal dysfunction (no. of cases)	16	6	0.003
Encephalopathy	6	1	NS
Haematological dysfunction	16	21	NS
Pulmonary dysfunction (no. of cases)	16	11	0.05
Atelectasis (no. of cases)	6	0	0.012
Pneumonia (no. of cases)	8	3	0.031
Pleural effusion (no. of cases)	12	10	NS
Metabolic acidosis (no. of cases)	7	0	0.006
Exitus (no. of cases)	6	0	0.012

*Rate of complications during the whole treatment period.

Table IV. Average time for the development of the complications in operated patients.

Intervention/complications	Days from admission
Surgical intervention	6.87
Renal dysfunction	5.92
Pulmonary dysfunction	11.63
Atelectasis	11.5
Pneumonia	17.25
Metabolic acidosis	13.14
Exitus	28.67

systemic inflammatory response as a result of the interplay of the numerous cytokines [17]. The clinical and pathophysiological manifestation of the systemic inflammatory response and end organ dysfunction are similar in the clinical course of SAP and sepsis [18,19]. Increased permeability of the capillary network and accumulation of fluid in the extravascular compartment are among the most characteristic features of the excessive excretion of pro- and anti-inflammatory cytokines [17]. Sequestration of the enzymatically rich fluid in the retroperitoneal space and/or intraperitoneally, accompanied by visceral oedema, is typical in SAP due to the above-mentioned cytokine effects. This mechanism is involved in the development of the abdominal compartment syndrome. Sustained increase of the IAP affects most intra-abdominal organs, and negative consequences of the intra-abdominal hypertension can be observed when IAP goes beyond 15 cm/H_2O. Microcirculation of the gastrointestinal tract can be affected severely when IAP reaches $\geq$25 cm H_2O [8]. Our results demonstrate strong association between sustained increase of the IAP and deterioration of the clinical course in patients with SAP. Elevation of the IAP was related to progression of organ dysfunction, especially when the abdominal compartment reached grade III–IV. It is not surprising that pulmonary and renal functions were affected most severely. Another negative consequence was observed when commencing enteral nutrition – tolerance of the enterally provided formula was poor in such cases. Although

Table V. Average interval from admission until development of complications and death.

Type of complications	Number of cases*	Days from admission
SIRS	5	4.5
MODS	6	2.5
Renal dysfunction	5	1
Pulmonary dysfunction	3	17
Atelectasis	3	1
Metabolic acidosis	4	1
Sepsis	1	26
Encephalopathy	3	20.67
Exitus	6	28.67

MODS, multiple organ dysfunction syndrome; SIRS, systemic inflammatory response syndrome.
*Data reflect the clinical course of six patients who died.

our study was not designed for particular assessment of the enteral feeding in SAP patients, the available data gave us a practical suggestion about impairment of the bowel function and low tolerance of the enterally provided feeding when IAP reaches nearly 20 cm/H_2O. Taken together, our data support previously reported recommendations that well-designed fluid replacement strategy based on adequate colloid/crystalloid composition and organ support facilitates reduction of the oedema and improves microcirculation [20]. Reduction of the third space and elimination of cytokines could also be achieved by application of RRT in the most severe cases [21]. Successful complex conservative treatment can result in gradual decrease of the IAP. According to our experience, prevention of the increased IAP is a rather important goal of the conservative treatment in patients with SAP, and surgical treatment should be avoided if possible. Surgical interventions, generally accepted for the reduction of the abdominal compartment in trauma patients, are difficult to apply directly to SAP patients. Although there is some controversial experience with this, the results are not very encouraging [22]. Our data are in parallel with the abovementioned findings. All lethal outcomes were associated with sustained increase of the IAP over 25 cm/H_2O and early surgical intervention. At the same time, dynamics of the IAP were not considerably affected by surgical exploration of the abdominal cavity, but most complications unfortunately occurred after surgical intervention in our series.

Despite the well-established fact that infection of necrosis is a major risk factor for the development of MODS, there is a subgroup of patients with sterile necrosis who develop progressive MODS. The new term 'early severe pancreatitis' was used to describe this category of patients [23,24]. Other triggering factors rather than infection could be responsible for the development of MODS in these cases. According to our observation, overwhelming SIRS with development of the abdominal compartment grade III–IV could be the pathophysiological link to the development of MODS in early SAP. Therefore prevention of the development of the abdominal compartment syndrome could be rational from the strategic point of view. Our data support the common opinion that early recognition of SAP patients requiring pulmonary and renal support is crucial and ICU management is the best option for this category of patients. Timely complex conservative strategy including control of the IAP improves overall treatment results, and shortens ICU and hospital stay.

Conclusion

Development of organ dysfunction in severe acute pancreatitis could be associated with increased IAP. Marked sustained grade III increase of IAP should be considered as an indicator for revision of the treatment modalities. Elevation of IAP over 25 cm/H_2O should not be considered the single indication for emergency decompressive laparotomy. Aggressive conservative treatment including isovolaemic haemodilution and CVVH rather than surgical intervention is recommended, particularly in the most severe cases.

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