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## ANESTHESIA & ANALGESIA | RESEARCH ARTICLE

# Relavance of peritoneal drainage fluid lactate level in patients with intra-abdominal hypertension

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**Abstract:** *Objective:* The aim of this study was to assess the effect of intra-abdominal hypertension (IAH) on peritoneal fluid lactate, local and systemic organ dysfunctions in patients after major abdominal surgery. *Methods:* In this prospective study, 26 patients were followed in the surgical intensive care unit. The lactate in peritoneal drainage fluid was analyzed 24 h after surgery concurrently with diuresis, renal FG, APP, creatinine clearance, bilirubin, AST, ALT, prothrombin time, CVP, cardiac index, PaO<sub>2</sub>, BE, arterial pH, arterial lactate, ScvO<sub>2</sub>, FiO<sub>2</sub>/pO<sub>2</sub> ratio, oxygen delivery, MAP and APACHE II. In the procedure 1 ml of peritoneal drainage fluid was drawn out from drainage catheter placed in abdominal cavity at the end of the operation. IAH has been defined as a peak intra-abdominal pressure (IAP) value of  $\geq 12$  mm Hg, at a minimum, as two standardized measurements obtained 1–6 h apart. *Results:* There were 16 patients with IAP  $> 12$  mm Hg and 10 patients with IAP  $< 12$  mm Hg. The mean IAP in groups was  $18.02 \pm 7.00$  vs.  $8.00 \pm 1.80$  mm Hg,  $p < 0.05$ , respectively. There are three major findings: a selective sensitivity of various organs dysfunction to the IAH level; the increase of IAP leads to lactate hyperproduction in abdominal drainage fluid ( $12.60$  vs.  $9.90$  mmol/L,  $p < 0.05$ ; and the systemic oxygen delivery was unaltered despite worsening of the local and systemic parameters caused

### ABOUT THE AUTHORS

Natasa Kovac, MD, is an anaesthesiologist and intensive care subspecialist, consultant in anaesthesiology and intensive care in UHC Zagreb. The author designed the study and wrote the manuscript which is part of her doctoral thesis.

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### PUBLIC INTEREST STATEMENT

In this study we searched for a new diagnostic parameter in surgical intensive care units in patients after major abdominal surgery. The major abdominal surgery are bowel resection due to tumor, strangulation, bleeding, gastric and duodenal surgery, oesophageal, pancreatic and liver surgery. Following such type of operation many patients developed intraabdominal hypertension (IAH) which could be detrimental, and life threatening. Our finding suggested that lactate in peritoneal drainage fluid could be useful diagnostic parameter that indicate pathophysiologic events in abdomen after surgery. In conclusion we can summarize the main findings of the study: (1) The liver is more resistant to increase of the IAP than kidney, (2) the lactate concentration in peritoneal drainage fluid is elevated in patients with IAH after major abdominal surgery, (3) Oxygen delivery, cardiac index and arterial lactate concentration remain in normal range despite increase of lactate in abdominal drainage fluid. Therefore, clinical monitoring of local lactate production may have a potential predictive and prognostic value.

by IAH. *Conclusion:* The lactate level in peritoneal drainage fluid may be an indicator of intra-abdominal dysfunction in surgical patients with IAH. Clinical monitoring of local lactate production may have a potential predictive and prognostic value.

**Subjects:** Gastroenterology; Anesthesiology; Critical Care Medicine; Surgical Anesthesia; Surgery; Gastrointestinal & Abdominal Surgery

**Keywords:** intra-abdominal pressure; intra-abdominal hypertension; abdominal compartment syndrome

## 1. Introduction

Intra-abdominal hypertension (IAH) frequently develops in patients with an acute abdomen syndrome caused by ileus, intestinal perforation, ruptured abdominal aneurysm, peritonitis, acute pancreatitis and some other non-traumatic as well as trauma-caused conditions (Malbrain et al., 2006; McNelis et al., 2002; Muckart, Ivatury, Leppaniemi, & Smith, 2006). Clinical correlation studies indicated that intra-abdominal pressure (IAP) above 12 mm Hg compromises the regional blood flow and reduces splanchnic tissue perfusion, thus producing tissue hypoxia, intestinal swelling and dysfunction of other organs (Ivatury & Diebel, 2006; Kovač, Širanović, & Mazul-Sunko, 2007; Raeburn & Moore, 2006; Surgue, Hallal, & D'Amours, 2006). The IAH progression leads to the abdominal compartment syndrome (ACS). A variety of dysfunctions are triggered, including bowel microcirculation dysfunction, loss of intestinal barrier, retroperitoneal and visceral edema, as well as an induction of severe inflammatory response, systemic inflammatory response syndrome (SIRS), and multiorgan dysfunction syndrome (MODS) (Benninger et al., 2012; Cheng et al., 2013; Doty et al., 2002; Jakob et al., 2000; Maddison, Karjagin, Tenhunen, & Starkopf, 2012; Reintam, Parm, Kitus, Starkopf, & Kern, 2008).

### 1.1. Physiological and pathophysiological intra-abdominal pressures

Normally the average intra-abdominal pressure is about 0 mm Hg, and some physiological states such as morbid obesity (BMI > 32 kg/m<sup>2</sup>) or pregnancy can cause a chronic increase in intra-abdominal pressure with no significant or mild pathophysiological consequences (Ivatury & Diebel, 2006; Kovac, 2016; Surgue et al., 2006). In the critically ill, IAP is often increased and also, abdominal surgery, bacterial translocation, sepsis, endotoxemia, organ failure, mechanical ventilation are associated with an increase in intra-abdominal pressure (Benninger et al., 2012; Raeburn & Moore, 2006; Surgue et al., 2006). Increased IAP can reach values that cause organ dysfunction, and these values vary from patient to patient, and that variability is due to individual reactivity and comorbidity.

The range of the IAP in the critically ill is between 5 and 7 mm Hg. Increased IAP may lead to IAH and/or ACS. According to the definition of World Society for Abdominal Compartment Syndrome (WSACS), IAH is a continuous increase in IAP above 12 mm Hg that is recorded in at least two measurements at intervals of 1 to 6 h.

According to the WSACS definition the ACS is defined as a continuously increased IAP above 20 mm Hg, which is associated with the new organ or organ systems dysfunction, with or without abdominal perfusion pressure (APP) <60 mm Hg. Since the values of the IAP may vary considerably in critically ill, among patients and individually the therapy should be adjusted accordingly. An alternative approach to increase the sensitivity of the IAP is to introduce APP as a therapeutic target. APP is the difference between mean arterial pressure and intra-abdominal pressure (APP = MAP – IAP). In clinical studies APP was observed in terms of one of prognostic vital factors with significant difference between the group of survivor and non-survivor patients with IAH/ACS. It was recommended to maintain APP above 50–60 mm Hg (Ivatury & Diebel, 2006; Kovač et al., 2007).

Hyperlactacidemia is a clinical marker of underlying ischemia and/or hypoxia whose degree of increase correlates with the severity of the illness (Jakob et al., 2000; Phypers & Tom Pierce, 2006; Wacharasint, Nakada, Boyd, Russell, & Walley, 2012). The gastrointestinal system, especially bowel mucosa shows great sensitivity to IAH. The sensitivity has been associated with the reduction of

mesenteric, hepatic and portal blood flow, decreased intramucosal perfusion and pH, increased permeability and loss of intestinal mucosal barrier (Crandall & West, 2006; Malbrain, 2008; Malbrain, Deeren, & De Potter, 2005; Phypers & Tom Pierce, 2006; Rezende-Neto et al., 2002; Wacharasint et al., 2012). Reduction of blood flow to all abdominal organs, and compression of mesenteric veins, with subsequent intestinal edema and ischemia, may lead to bacterial translocation, sepsis and multiorgan failure. Variety of mechanisms and their interaction contribute to full development of ACS (Cheatham, 2009; Cheatham et al., 2007; Malbrain, 2004; Malbrain & Wilmer, 2007; Malbrain et al., 2004, 2014).

The plasma lactate is used to detect and monitor hypoperfusion and as a prognostic indicator. Lactate production may be considered as an indicator of protective response by the body to allow cellular energy production to continue when tissue oxygen supply is inadequate for aerobic metabolism. The hypoxia inducible factor (HIF) is the sensor of low tissue oxygen that switches metabolism to anaerobic mode. The increase in plasma lactate concentration may develop due to an absolute and/or relative tissue oxygen deficiency.

Energy metabolism switching induced by IAH has been corroborated in different experimental models. Benninger et al. (2012) evaluated microdialysis of rectus abdominis muscle (RAM) for early detection of subclinical organ dysfunction in a porcine model of IAH. Microdialysis showed significant increase in lactate/pyruvate ratio in higher IAH group (Klaus, Heringlake, Gliemroth, Bruch, & Bahlmann, 2002; Sommer & Larsen, 2004; Tenhunen, Jakob, Ruokonen, & Takala, 2002; Ungerstedt, Nowak, Ericzon, & Ungerstedt, 2003). Intra-abdominal pressure-induced ischemic metabolic changes are detected more rapidly and pronounced by microdialysis of the RAM when compared with intra-abdominal organs. IAH during laparoscopic surgery, even for a relatively short duration, is associated with metabolic changes in the abdominal wall muscle tissue (Maddison et al., 2012; Meier et al., 2007). In the animal model, the occlusion of superior mesenteric artery for 1 h induces a marked rise of lactate in the perfusate but not in blood (Ljungdahl, Rasmussen, Raab, Hillered, & Haglund, 1997). Very similar results were shown by Tenhunen et al. (2002) in an animal study where they observed influence of low systemic hypoperfusion on gut luminal lactate. The work of Reynaert et al. (1984) suggested that the lactate level in peritoneal fluid could be an early diagnostic tool of peritoneal infection. In veterinary medicine peritoneal fluid lactate has been used as a marker of intestinal ischemia and is a better predictor of intestinal ischemia secondary to a strangulation obstruction than blood lactate (Dabareiner, White, & Donaldson, 2001; Moore, Muir, & Granger, 1995; Snyder, 1989).

## 2. Methods

### 2.1. Patients and methods

The Ethics Committee of University Hospital “Sestre milosrdnice”, Zagreb, Croatia, approved the conduct of the study (EP-03-1/08). In this longitudinal/prospective single-centre observational study all adult patients who were admitted to the surgical ICU from September 2005 to April 2006 after major abdominal surgery due to sigmoid perforation ( $n = 2$ ), ileus caused by tumor ( $n = 3$ ), bulbostenosis ( $n = 1$ ), bleeding gastric ulcer ( $n = 1$ ), abdominal aortic aneurysm ( $n = 1$ ), oesophageal tumor ( $n = 1$ ), colon tumor ( $n = 5$ ), pancreatic cyst ( $n = 1$ ) or tumor ( $n = 1$ ), gastric tumor ( $n = 6$ ), gastric ulcer ( $n = 2$ ) and duodenal ulcer ( $n = 2$ )—in total, 26 patients were included in the study. The patients included in the study have had to stay at least 24 h in the ICU, and had no previous liver or kidney disease including cirrhosis, hepatitis, and liver resection, then chronic renal disease or renal insufficiency. On admission the following data were recorded: age, sex, Acute Physiology and Chronic Health Evaluation (APACHE II) score, IAP value and type of admission: elective or urgent (Table 1). The renal FG, diuresis, creatinine clearance, bilirubin, ALT, AST, PT, and fluid gain were recorded on daily basis. The arterial blood gases, IAP, APP, MAP, CVP, ScV<sub>2</sub>, CI, serum lactate, FiO<sub>2</sub>/pO<sub>2</sub> ratio and peritoneal drainage fluid lactate were recorded and measured three times a day at six hours apart. According to the definition of WSACS, IAH was considered when an IAP was persistently 12 mm Hg or above that is recorded in at least two measurements at intervals of 1 to 6 h (Malbrain et al., 2006). Then average values of those parameters were calculated. Blood gases, arterial lactate and peritoneal

**Table 1. Baseline characteristics of patients**

Variable	HIAP group	NIAP group	p value
N (patients)	16 (61.50%)	10 (38.50%)	
Age (year)	69 ± 9	61 ± 10	
Male	2 (75%)	7 (70%)	
Female	4 (25%)	3 (30%)	
Mean IAP male	17.43 ± 8.10 mm Hg	8.89 ± 1.80 mm Hg	<0.05
Mean IAP female	13.70 ± 6.00 mm Hg	8.30 ± 1.90 mm Hg	<0.05
APACHE II score (points)	17 ± 8.70	11 ± 5.70	<0.05
Urgent surgery - mean IAP	18.50 ± 8.00 mm Hg	/	
Elective surgery - mean IAP	14.99 ± 7.10 mm Hg	8.22 ± 1.80 mm Hg	<0.05

Abbreviations: HIAP = high intra-abdominal pressure, NIAP = normal intra-abdominal pressure, APACHE = acute physiology and chronic health evaluation, IAP = intra-abdominal pressure.

drainage fluid lactate levels were measured using the blood gas analyzer (GEM Premier 3000, Instrumentation Laboratory). According to the IAP values, patients were sorted into the two groups, the high intra-abdominal pressure (HIAP) and the normal intra-abdominal pressure (NIAP). The first one consisted of patients with IAP > 12 mm Hg that is recorded in at least two measurements at intervals of 1 to 6 h, whereas the NIAP-patients were those with IAP < 12 mm Hg. Measurements were done by transvesical technique with instillation of 25 ml of normal saline, according to the procedure described by World Society of Abdominal Compartment Syndrome (Malbrain et al., 2006). Shortly thereafter, the zero point was established at mid-axillary line in supine position at the end of expiration. The average of daily IAP values was used to select patients into the NIAP or HIAP group. Patients who had one IAP below 12 mm Hg and another above 12 mm Hg were allocated in NIAP group. The measurements were repeated as long as the patients were in ICU for at least 72 h. The patients who overlapped in both groups were excluded.

The data are divided into the groups that represent local parameters (diuresis, renal FG, APP, CrCl, bilirubin, AST, ALT, PT, lactate in drainage fluid (lactate/D)) and systemic parameters (CVP, CI,  $paO_2$ , BE, arterial pH, arterial lactate (lactate/S),  $SvO_2$ ,  $PaO_2/FiO_2$ ,  $DO_2$ , arterial carbon dioxide partial pressure ( $pCO_2$ ), MAP) (Table 2). The APACHE II score was used to assess clinical state severity along with the clinical outcomes, survivors vs. non-survivors.

The parameters which were measured three times a day were taken and measured at the same time: arterial blood was drawn for blood gases analysis, and 1 ml of peritoneal drainage fluid was drawn out from drainage catheter which was placed in abdominal cavity at the end of operation. MAP was measured directly via arterial line. APP was calculated according to the formula  $APP = MAP - IAP$ . Renal filtration gradient (FG) represents a mechanical pressure force across the glomeruli. FG is defined as the difference between the glomerular filtration pressure (GFP) and proximal tubular pressure (PTP), thus  $FG = GFP - PTP$ . FG was calculated according to IAH values as  $FG = MAP - 2 \times IAP$ , but when the IAP is increased, the PTP can be equated with the IAP, while GFP is estimated by the difference between MAP and IAP (Surgue et al., 2006). The CI values were estimated via PICCO hemodynamic monitoring (PULSION Medical Systems). The patients were following up while in the ICU at least 72 h.

## 2.2. Statistical analyses

This was a pilot study, and prior correlation between peritoneal lactate level and intraabdominal hypertension in humans were not available. Therefore we were not able to perform any power calculations for sample size estimation. The results were analyzed by Student's T-test for independent samples, the Spearman rank-order correlation coefficient for nonparametric variables. All the tests

**Table 2. Comparison of local and systemic pathophysiological effects of IAH in the NIAP group and the HIAP group**

	HIAP group (IAP ≥ 12 mm Hg)	NIAP group (IAP < 12 mm Hg)	p-value
Mean IAP (mm Hg)	18.02 ± 7.00	8.00 ± 1.80	<0.05
<i>Local parameters</i>			
Diuresis (ml/daily)	2500 ± 1500	3700 ± 1800	<0.05
APP (mm Hg)	63.09 ± 19.82	81.03 ± 21.03	<0.05
FG (mm Hg)	47.01 ± 23.03	75.01 ± 21.02	<0.05
Creatinine clearance (ml/min)	44.03 ± 34.02	61.03 ± 50.01	<0.05
PT (%)	80.02 ± 22.01	79.00 ± 18.01	0.84
Bilirubin (µmol/L)	20.01 ± 31.02	18.03 ± 1.00	0.41
AST (mmol/L)	43.16 ± 28.86	30.92 ± 27.68	0.08
ALT (mmol/L)	29.83 ± 24.68	23.05 ± 20.08	0.27
Lactate D (mmol/L)	12.60 ± 7.01	9.90 ± 5.02	<0.05
<i>Systemic parameters</i>			
CVP (mm Hg)	7.00 ± 3.00	3.00 ± 2.00	<0.05
APACHE II	17.00 ± 8.70	11.00 ± 5.70	<0.05
CI (L/min/m <sup>2</sup> )	4.10 ± 0.90	4.20 ± 0.90	0.64
pCO <sub>2</sub>	5.60 ± 2.60	5.20 ± 0.90	0.29
BE (mmol/L)	-8.00 ± 4.30	-3.00 ± 4.70	<0.05
Arterial pH	7.27 ± 0.09	7.35 ± 0.09	<0.05
Arterial lactate (mmol/L)	1.90 ± 1.00	1.40 ± 2.00	0.84
SvO <sub>2</sub> %	70.00 ± 9.80	70.00 ± 7.00	0.69
PaO <sub>2</sub> /FiO <sub>2</sub>	264 ± 117	252 ± 113	0.58
DO <sub>2</sub> (ml/min/m <sup>2</sup> )	516 ± 112	533 ± 110	0.39
MAP (mm Hg)	82.00 ± 17.20	93.00 ± 19.70	<0.05

Note: Data are reported as mean ± SD (standard deviation).

Abbreviations: APP = abdominal perfusion pressure, FG = filtration gradient, PT = prothrombin time, alanine aminotransferase (ALT), aspartate aminotransferase (AST), lactate D = lactate concentration in peritoneal drainage fluid. CVP = central venous pressure, APACHE = acute physiology and chronic health evaluation, BE = base excess, CI = cardiac index, pCO<sub>2</sub> = arterial carbon dioxide partial pressure, SvO<sub>2</sub> = oxygen saturation in central venous blood, PaO<sub>2</sub>/FiO<sub>2</sub> = ratio between oxygen arterial partial pressure and fractional concentration of inspired oxygen, DO<sub>2</sub> = oxygen tissue delivery, MAP = mean arterial pressure.

were interpreted relative to the significance threshold  $p = 0.05$  and statistical significance was considered below the significance threshold value.

### 3. Results

Twenty-six patients met the inclusion criteria. According to the measured IAP values patients were sorted into the NIAP group and the HIAP. There were 16 patients in HIAP group and 10 in NIAP group. There were 234 parameters in total from 26 patients, which were recorded and measured three times a day at six hours apart. When the average value was calculated, there were 78 data left. Patients' demographic data and type of surgery elective vs. urgent are listed in Table 1. The IAH effects of abdominal organ dysfunction were compared in two groups (Table 2). We found statistically significant differences between the HIAP and NIAP groups with respect of daily diuresis, APP, FG, creatinine clearance, and lactate in peritoneal drainage fluid, but not in prothrombin time, bilirubin and transaminase values. These data imply that liver functions may be more resistant to IAP increases than kidney functions (Table 2).

**Table 3. Comparison of IAP, APP, lactate in peritoneal drainage fluid and arterial lactate according to survival**

	Survivors	Non-survivors	p-value
Number of patients	18	8	
IAP (mm Hg)	13 (8–25)	17.9 (3.1–47)	<0.05
APP (mm Hg)	77 (57–103.7)	63.3 (47–103)	<0.05
Lactate D value (median) (mmol/L)	8.34 (0.8–24)	11.6 (0.75–33)	<0.05
Lactate S value (median) (mmol/L)	1.27 (0.5–3.27)	1.42 (0.2–14)	0.84
Lactate D/Lactate S	5.85	8.41	<0.05

Abbreviation: IAP = intra-abdominal pressure, APP = abdominal perfusion pressure, lactate S = lactate concentration in serum, lactate D = lactate concentration in peritoneal drainage fluid.

In parallel, the systemic physiological effects of IAH were analyzed and summarized in Table 2. The HIAP patients had altered hemodynamic parameters including the increase of CVP, and decrease of MAP. They developed a mild acidosis and had worse APACHE score. However, there was no influence of the IAH on the cardiac index, venous gas pressures, saturation and delivery of oxygen into the tissues.

Since the increase of IAP correlated to local and systemic derangements, we analyzed the IAH effects on survival of our patients. Clinical survival status at the ICU discharge was compared to the IAP values. According to survival criteria there were 18 patients who survived and 8 deaths in the ICU (Table 3). The median IAP value in survivors was 13 mm Hg (range 8.00–25) and in non-survivors 17.90 mm Hg (range 3.10–47),  $p < 0.05$ . The median APP was higher in survivors group than in non-survivors, 77 mm Hg (57–103.70) vs. 63.30 mm Hg (47–103),  $p < 0.05$ . Also, peritoneal lactate concentrations measured in the abdominal drainage fluid were significantly different among groups - survivors had median 8.34 mmol/L and non-survivors 11.6 mmol/L,  $p < 0.05$ . We reasoned that intra-abdominal hyperproduction of lactate should be due to local intraabdominal processes triggered by IAH and reduced APP. Namely; increased local lactate production does not lead to significant systemic hyperlactacidemia. Measured arterial lactate in survivors had median 1.27 mmol/L (range 0.5–3.27), and non-survivors 1.42 mmol/L (range 0.20–14),  $p = 0.84$  (Table 3), presumably due to a still sufficient liver urea cycle metabolism under these conditions. The increase IAP was treated according to the management algorithm for IAH/ACS, mostly conservative which include: sedation and analgesia, nasogastric decompression, rectal decompression, gastro-colonic prokinetic agents, avoidance of excessive fluid resuscitation, diuretics, haemodialysis and organ support with vasopressors. The effects of intervention to lower IAP were not examined.

#### 4. Discussion

ACS is potentially lethal condition that may develop insidiously due to a critically increased IAH. Since the ACS is treatable disease process, surgical intensivists seek for monitoring biomarkers for timely prevention of IAH local and systemic harmful effects and its progression to ACS. In this study we studied the effect of IAH effects on peritoneal fluid lactate, local and systemic organ dysfunctions in patients after major abdominal surgery.

There are three main findings in our study. Firstly, the increase of IAP which caused kidney failure at the same time had a minimal effect on liver functions in the HIAP group. Secondly, the increase of IAP led to hyperproduction lactate in abdominal drainage fluid implying a worsening of local ischemic conditions and it is significantly higher in non-survivors. Thirdly, systemic hemodynamic parameters such as MAP and CVP were significantly changed and the arterial pH is lower, despite yet unaltered  $DO_2$ , CI and arterial lactate. All three findings may be useful in clinical management of patient's condition and they add up some facets to understanding of basic physiology of the IAH-induced derangement of local and systemic functions.

*The first finding* was that implies a selectivity of organ damage to the gradual IAH increase. Kidney failure proceeds ahead of liver dysfunction early in the development of the syndrome. The HIAP group patients developed kidney dysfunctions expectedly. Namely, numerous published studies have reported high kidney sensitivity to IAH. IAP of 8–12 mm Hg causes kidney hypoperfusion, oliguria develops at IAH over 15 mm Hg, and anuria is common once the pressure exceeds 25–30 mm Hg (Dalfino, Tullo, Donadio, Malcangi, & Brienza, 2008; De Waele & De Laet, 2007; Moore-Olufemi et al., 2005; Shear & Rosner, 2006). Clinical manifestation of kidney dysfunction (a decrease of glomerular filtration and creatinine clearance capacity as well as reduction of urine output) is inversely correlated to the IAP elevation, and starts already at the mild IAH values. Average IAP of 18 mm Hg caused kidney dysfunction in our study. Similar values were reported by Dalfino study of IAH that lead to acute renal failure (Dalfino et al., 2008). High sensitivity of kidney to the IAH may be due to double impact of IAP on renal functions. Firstly, IAH reduces blood flow in glomeruli and filtration rate. Secondly, IAH leads to an increase of tissue and nephron luminal pressure in the proximal tubules. These two effects synergize in development of kidney failure. These findings are consistent with other reports on rapid loss of filtration gradient due to rise of IAH (Malbrain, 2008; Surgue et al., 2006). De Waele and De Laet (2007) pointed out that the kidney is the most vulnerable organ to IAH because of its anatomic position. Chang et al. (2013) suggested that IAH has a significant pathological mechanism and potential independent risk factor of hepatorenal syndrome, implying an early kidney failure.

On the other side, however, the HIAP group patients' liver functions were within the normal range, despite the IAH. Obviously, those levels of IAH (18+/-7.00 mm Hg) were compatible with unaltered serum liver enzymes, blood coagulability and bilirubin concentrations. It seems the liver is more resistant to the IAH rise in comparison to kidney injury triggering. It appears that IAH damages liver at a higher pressure rise.

It has been reported that hepatic arterial, portal, and microvascular blood flow are affected at higher IAH values in comparison with kidney blood flow (Chang et al., 2013). Effects of intra-abdominal pressure on liver function were researched by several groups. Turan et al. reported that IAH rise to 19–22 mm Hg caused significant reduction of indocyanine green plasma disappearance rate (ICG-PDR) and significant increase of liver enzymes activity in comparison to IAP of 12–13 mm Hg (Inal et al., 2011; Malbrain et al., 2012). Animal and human studies have shown impairment of hepatic cell function and liver perfusion even with only moderately elevated IAP. Cytochrome P450 function may be altered in IAH/ACS, which may have important clinical implications regarding drug dosage. Increased IAP leads to a decreased hepatic blood flow and a decreased venous portal flow and increases the portal collateral circulation causing physiological effects with decreased lactate clearance, altered glucose metabolism and altered mitochondrial function (Wendon, Biancofiore, & Anzinger, 2006).

*The second finding* of lactate elevation in peritoneal drainage fluid with no plasma lactate increase may have a clinical relevance. Peritoneal drainage fluid lactate is elevated in patients with high IAP and low APP and it correlates with the extent of the IAH. It is not related to arterial lactate, CI nor DO<sub>2</sub>. Therefore, it seems to be a direct consequence of a local intra-abdominal ischemia and it might serve an early sign of pathological events in surgical patients with IAH after abdominal surgery. Increase of lactate in peritoneal drainage fluid may have predictive values, because there is a statistically significant correlation among survivors and non-survivors and level of lactate in peritoneal drainage fluid, as shown in Table 3. Local ischemic conditions within the postoperative abdominal tissues are intensified by the IAH. Metabolic anaerobic shift reflects a deterioration of local blood perfusion due to limited abdominal wall compliance and IAH development. Therefore we would like to conclude that drainage fluid lactate may be an early sign of IAH induced pathology. On the other side, both animal and human ACS studies have shown a beneficial effect of abdominal decompression laparotomy and correction of hyperlactacidemia (Cheatham et al., 2007; Ivatury & Diebel, 2006; Malbrain et al., 2006; McNelis et al., 2002; Muckart et al., 2006). The same procedure quickly led to the reversion of cardiopulmonary and abdominal dysfunctions, as well.

Lactate rise in drainage fluid may be very sensitive indicator of local intraabdominal IAH-related pathological processes. We reasoned that majority of those locally produced lactates are easily washed away into the draining fluid. The other part is metabolized by liver and thus do not rich the systemic circulation. Therefore, the drainage fluid should be an appropriate sample to be analysed for early events in surgical patients with the IAH. Since it is readily available in postoperative period, draining fluid approach has a practical advantage, as well. In this study, limited number of measurements does not allow a strong generalization, but it points towards an important phenomenon, not previously reported in literature. More extensive study may prove draining fluid lactates as potential early biomarker of IAH-induced processes in the abdomen.

*The third finding* was that of unaltered systemic oxygen delivery, cardiac index and arterial lactate despite the worsening of APACHE II score, lower MAP and higher CVP in the HIAP group. The extra-abdominal etiopathogenesis triggered by the IAH often affects respiration system, hemodynamic and central nervous system functions. According to the literature derangements of those systems are mediated by inflammatory cascade, cytokines, endotoxins, endogenous toxic substances (etc.) (Fineschi et al., 2006; Oda, Ivatury, Blocher, Malhotra, & Sugerman, 2002). One may expect that HIAP systemic functions disorders reflect the specific stage in development towards fully expressed ACS. Since MAP is the major blood perfusion force, one would expect a progressive reduction of oxygen delivery and tissue systemic ischemia to develop. However, reduced MAP in the HIAP group was sufficient for an unaltered oxygen delivery. This may be due to various compensatory responses in the extra-abdominal organs (like Bohr Effect, 2,3-diphosphoglycerate, etc.). In addition it has been reported that other mechanisms (e.g. cytokines, endogenous toxic substances) may be responsible for worsening of the clinical indices along with normal oxygen delivery (Clark & Coopersmith, 2007; Holland et al., 2005; Solligård et al., 2008).

The systemic acidosis despite normolactacidemia in HIAP group patients may be due to different acidogenic processes in the body due to fluids therapy. Daily fluid administration in both group of patients and total intake in HIAP group was significantly higher ( $5,174.98 \text{ ml} \pm 1,298.59$ ) in comparison with NIAP group ( $4,607.35 \text{ ml} \pm 1,395.07$ ),  $p < 0.05$ . But total losses were lower in HIAP than in NIAP group,  $3,540.16 \text{ ml} \pm 1,746.65$  vs.  $4,469.39 \text{ ml} \pm 2,162.89$ ,  $p < 0.05$ . This could be explained by reduced kidney function and lower diuresis already mentioned in the first finding but also with the type of administrated fluid. Theoretically the excess of chloride might contribute to development of systemic acidosis.

In conclusion the authors would like to emphasize that the IAH induces the intra-abdominal pathology with gradual function deterioration of individual organs. Hypoperfusion of intra-abdominal organs due to IAH caused disturbance of fluid balance and dynamics on the capillary wall (Starling capillary forces derangement). In addition, IAH produces the Starling resistor effect, in which the external pressure to arteries and veins results in blood flow reduction (Kamm, 1987). The same applies to the lymph dynamics. Both blood and lymph fluid disorders contributed to a variety of clinical presentations. Mild, moderate and severe IAH grades correlate with a spectrum of symptoms and dysfunctions, as well as with the severity of the condition. Short intermittent IAH may produce no dysfunction (like within the normal physiologic conditions such as coughing, defecation, exercise and Valsalva manoeuvre). On the other hand, a continuous IAH leads to a serious clinical problem (Cheatham, 2009; Cheng et al., 2013; Malbrain & Wilmer, 2007; Raeburn & Moore, 2006; Rezende-Neto et al., 2002; Surgue et al., 2006). Protracted IAH above 50 mm Hg is inconsistent with life.

For intensivists' daily practice the abdominal drainage fluid lactate may be important marker of immediate clinical interest and diagnostic value.

The systemic extra-abdominal derangements and morbidities induced by IAH are even more polymorphic than the intra-abdominal ones. Despite normal oxygen delivery and normolactacidemia disorders of hemodynamic and general clinical performance are worsened.

We hope that these data and interpretation shine some additional light into the complexity of IAH etiopathogenesis and necessity of careful monitoring of functional systems in ICU.

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The authors declare no competing interest.

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