

# Effect of intraabdominal hypertension on splanchnic blood flow in children with appendicular peritonitis

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## Abstract

**Background and Aims:** Intraabdominal hypertension (IAH) is poorly diagnosed condition that cause splanchnic hypoperfusion and abdominal organs ischemia and can lead to multiple organ failure. There are no scientific data regarding effect of intraabdominal pressure (IAP) on splanchnic circulation in children.

**Material and Methods:** Ninety-four children after surgery for appendicular peritonitis were enrolled in the study. After IAP measurement children were included in one of two groups according IAP levels: "without IAH" ( $n = 51$ ) and "with IAH" ( $n = 43$ ). Superior mesenteric artery (SMA) and portal vein (PV) blood flows ( $BF_{SMA}$ ,  $BF_{PV}$  mL/min) were measured, and SMA and PV blood flow indexes ( $BFI_{SMA}$ ,  $BFI_{PV}$ , mL/min\*m<sup>2</sup>) and abdominal perfusion pressure (APP) were calculated in both groups.

**Results:** Median  $BFI_{SMA}$  and  $BFI_{PV}$  in group "with IAH" were lower by 54.38% ( $P < 0.01$ ) and 63.11% ( $P < 0.01$ ) respectively compared to group "without IAH". There were strong significant negative correlation between IAP and  $BFI_{SMA}$  ( $r_s = -0.66$ ;  $P < 0.0001$ ), weak significant negative correlation between IAP and  $BFI_{PV}$  ( $r_s = -0.36$ ;  $P = 0.0001$ ) in group "with IAH" and weak significant negative correlation between IAP and  $BFI_{SMA}$  ( $r_s = -0.30$ ;  $P = 0.0047$ ) in group "without IAH". There were no statistically significant correlations between IAP and  $BFI_{PV}$  in group "without IAH", between  $BFI_{SMA}$  and APP in both groups and between  $BFI_{PV}$  and APP in both groups.

**Conclusion:** Elevated IAP significantly reduces splanchnic blood flow in children with appendicular peritonitis.  $BFI_{SMA}$  and  $BFI_{PV}$  negatively correlate with IAP in these patients. There is no correlation between  $BFI_{SMA}/BFI_{PV}$  and APP in children with IAH due to appendicular peritonitis.

**Keywords:** Intraabdominal pressure, portal vein, splanchnic blood flow, superior mesenteric artery

## Introduction

Intraabdominal hypertension (IAH) and abdominal compartment syndrome (ACS) frequently remain unrecognized in critically ill patients. This can be due to lack of familiarity among health care providers with these conditions. ACS is associated with 90-100% mortality if not recognized and treated promptly. Besides, elevated intraabdominal pressure (IAP) is reported as independent predictor of mortality among critically ill patients.<sup>[1,2]</sup>

Increased IAP leads to gastrointestinal, cardiovascular, respiratory, renal, hepatobiliary and central nervous system disorders.<sup>[3]</sup>

Gastrointestinal system responds first when IAP rises. Increased IAP leads to splanchnic hypoperfusion caused by direct compression of abdominal vessels, low cardiac output and increased systemic vascular resistance. As IAP increases, abdominal perfusion pressure (APP)

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progressively decreases which can lead to abdominal organ ischemia. The literature data on effect of increased intraabdominal pressure on splanchnic circulation were based mainly on experimental studies.<sup>[4]</sup> Splanchnic blood flow in children with IAH has not been studied well. We hypothesized that there would be correlation between the intraabdominal pressure level and the severity of decreased splanchnic circulation.

The aim of the study was analyzing the effects of intraabdominal pressure level on the state of splanchnic blood flow in children with appendicular peritonitis. The primary objective was to study of splanchnic circulation level in children with IAH and without IAH due to appendicular peritonitis. The secondary objective was analyzing the correlation between intraabdominal pressure and splanchnic blood flow.

## Material and Methods

The prospective observational study was approved by local IRB: Lviv Regional Children's Hospital Ethics Committee (Protocol#3-1-2018, dated January 10, 2018, chairperson O. Burda, MD, PhD). The study was registered in the Australian New Zealand Clinical Trials Registry as ACTRN12618001716257 (available on: <http://www.ANZCTR.org.au/ACTRN12618001716257.aspx>).

The inclusion criteria of the study were as follows: (1) early postoperative period after appendicular peritonitis surgery; (2) age 3–18 years; (3) no contraindications to IAP measurement through the bladder; (4) parental informed consent for study participation.

Ninety-four children after surgical intervention for appendicular peritonitis were enrolled in the study. Surgery in all children included laparotomy, appendectomy (in some cases partial omentum resection), lavage and drainage of the abdominal cavity. After IAP measurement children were included in one of two groups according IAP levels: “without IAH” ( $n = 51$ ) and “with IAH” ( $n = 43$ ) in which IAP was less than 10 mm Hg and more than 10 mm Hg respectively. Children in groups did not differ by age, gender and anthropometric data. Demographic data of enrolled children are shown in Table 1.

All children were admitted in PICU after surgery. Postoperative treatment included antibacterial therapy, correction of electrolyte and fluid status, nasogastric decompression, pain management. All children had no enteral nutrition prior to gastrointestinal passage restoration. All children had standard

postoperative monitoring (temperature, ECG, SpO<sub>2</sub>, blood pressure, urinary output, nasogastric drainage volume, bowel sounds, defecation).

IAP was measured 4 times per day. IAP measurement was performed according to standard technique based on the WSACS consensus definitions.<sup>[5]</sup>

APP (mmHg) was calculated using following equation:  $APP = MAP - IAP$ , were MAP is a mean arterial pressure.

Diameters of superior mesenteric artery (SMA) and portal vein (PV) and linear blood flow velocities in these vessels were measured using USG scanner (Hitachi™ EUB-525 PLUS, 3.5-5 MHz convex probe) 4 times per day simultaneously with IAP measurement. SMA was located in long axis just below the xiphoid process 1-2 cm distally from the its origin. PV was located in long axis in the right upper quadrant of the abdomen. The cross-sectional area (CSA, cm<sup>2</sup>) of vessels was calculated automatically. SMA and PV blood flows were measured using a real-time pulsed Doppler ultrasound method with Doppler angle below 60°. After achieving optimized Doppler signals for 10-20 seconds, five homogeneous cardiac cycles were measured. Systolic and diastolic velocities, and time-average mean velocity (TAMV, cm/sec) were registered. The volumetric blood flow (BF) of SMA and PV ( $BF_{SMA}$ ,  $BF_{PV}$ , ml/min) was calculated using following equation:  $BF = CSA * TAMV * 60$ , were CSA is cross-section area of vessels, TAMV is time-average mean velocity.<sup>[6]</sup> SMA blood flow index and PV blood flow index ( $BFI_{SMA}$ ,  $BFI_{PV}$ , ml/min\*m<sup>2</sup>) were calculated using following equation:  $BFI = BF/BSA$ , were BSA is body surface area. BSA was calculated using Mosteller's equation.<sup>[7]</sup>

Sample size was calculated for the primary outcome which is the level of splanchnic circulation in children with IAH and without IAH due to appendicular peritonitis, based on the previous study by Diebel *et al.*<sup>[8]</sup> which showed that the median superior mesenteric artery blood flow in domestic swine would be 128±27 ml/min (mean ±

**Table 1: Demographic data of enrolled children**

Groups	“without IAH” <i>n</i> =51	“with IAH” <i>n</i> =43
Age, months (median (25; 75 quartile))	103.2 (53.1; 136.4)	101.3 (49.7; 117.6)
Male/female, n/n	23/28	26/17
Body weight, kg (median (25; 75 quartile))	23.1 (14.4; 40.9)	21.8 (13.7; 38.6)
Height, cm (M±SD)	134.2±27.7	131.8±28.8

IAH - intraabdominal hypertension

standard deviation) in cases without IAH and  $94 \pm 28$  ml/min due to IAH. Taking a power of 90% and alpha error of 0.05, a minimum sample of 26 patients (13 patients in each group) was calculated. A total of 94 patients were included (51 patients in group “without IAH” and 43 patients in “IAH” group) to compensate for the possible dropouts from the study.

### Statistical analysis

Data with normal distribution were expressed as mean and standard deviation. Data with non-normal distribution were expressed as median and 25 and 75 quartiles. Data were analyzed using STATISTICA 8.0 software. Statistical significance of differences was assessed using Student's *t*-test for data with normal distribution and Mann-Whitney's *U* test for data with non-normal distribution. Correlations between variables were calculated using Spearman's correlation analysis and expressed as Spearman's correlation coefficient ( $r_s$ ). Differences and correlations were considered significant if *P* value was lower than 0.05.

### Results

Main study results are summarized in Table 2.

Median  $BF_{SMA}$  and  $BF_{PV}$  were significantly lower in group “with IAH”. Median  $BFI_{SMA}$  and  $BFI_{PV}$  were significantly lower in group “with IAH” as well. The reduction of blood flow indexes in group “with IAH” compared to group “without IAH” was by 54.38% ( $P < 0.01$ ) and 63.11% ( $P < 0.01$ ), respectively.

MAP was higher in group “with IAH”. APP did not differ between groups.

Weak significant negative correlation between IAP and  $BFI_{SMA}$  ( $r_s = -0.30$ ;  $P = 0.0047$ ) was observed in group “without IAH” [Figure 1]. Strong significant negative correlation between IAP and  $BFI_{SMA}$  ( $r_s = -0.66$ ;

$P < 0.0001$ ) and weak significant negative correlation between IAP and  $BFI_{PV}$  ( $r_s = -0.36$ ;  $P = 0.0001$ ) was observed in group “with IAH” [Figures 2 and 3]. There were no statistically significant correlations between IAP and  $BFI_{PV}$  ( $r_s = -0.04$ ;  $P = 0.71$ ) in group “without IAH”, between  $BFI_{SMA}$  and APP in both groups ( $r_s = 0.003$ ;  $P = 0.98$  in group “without IAH”,  $r_s = 0.029$ ;  $P = 0.77$  in group “with IAH”) and between  $BFI_{PV}$  and APP in both groups ( $r_s = -0.106$ ;  $P = 0.33$  in group “without IAH”,  $r_s = -0.098$ ;  $P = 0.32$  in group “with IAH”).

### Discussion

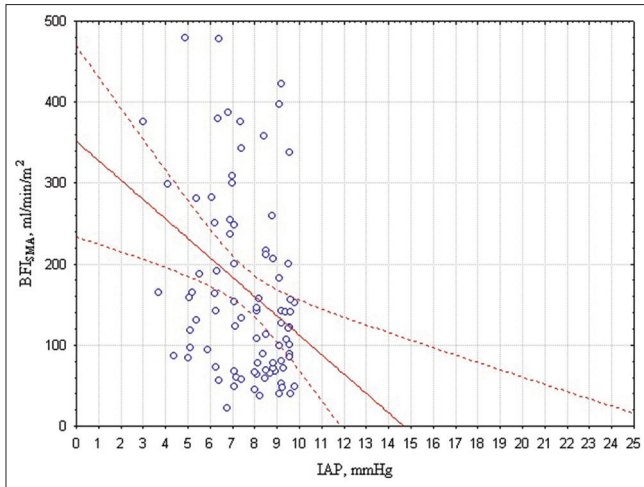
The majority of results on effect of IAH on splanchnic blood flow have been obtained in animal studies and/or with methods, which cannot be used in clinical practice, such as laser Doppler flowmetry, refractance spectrophotometry, infrared spectroscopy, biochemical markers, histological examination and others.

Experimental studies demonstrated  $BF_{SMA}$  impairment in animals with IAH. Diebel *et al.* showed that application of IAP of 20 mm Hg in pigs caused significant decrease in  $BF_{SMA}$  to  $73 \pm 22\%$  from baseline. Increasing IAP to 30 and 40 mm Hg led to  $BF_{SMA}$  reduction to  $48 \pm 25\%$  and  $31 \pm 15\%$  from baseline respectively.<sup>[8]</sup> Similar data was obtained in study of Avital *et al.* They demonstrated that  $BF_{SMA}$  significantly decreased over time (from  $299.8 \pm 185.2$  to  $242.0 \pm 149.9$  ml/min), as long as IAP was increased from 2 to 20 mm Hg in anesthetized pigs.<sup>[9]</sup> Kleinhaus *et al.* observed stepwise reductions of  $BF_{SMA}$  by 18%, 31%, 40%, and 49% from control after experimental increasing of intraperitoneal pressure by 10 mm Hg increments from 0 to 40 mm Hg in dogs.<sup>[10]</sup> Significant changes in  $BF_{SMA}$  were observed in Mogilner's *et al.* study with anesthetized rats. Inflation of air in peritoneal cavity to IAP of 3 and 6 mm Hg resulted in a 19% and 30% reduction in  $BF_{SMA}$  respectively compared to initial levels.<sup>[11]</sup> Kotzampassi *et al.* showed that application of IAP of 12 mm Hg in pigs which were ventilated with positive end-expiratory pressure led in 35% decrease in  $BF_{SMA}$ .<sup>[12]</sup>

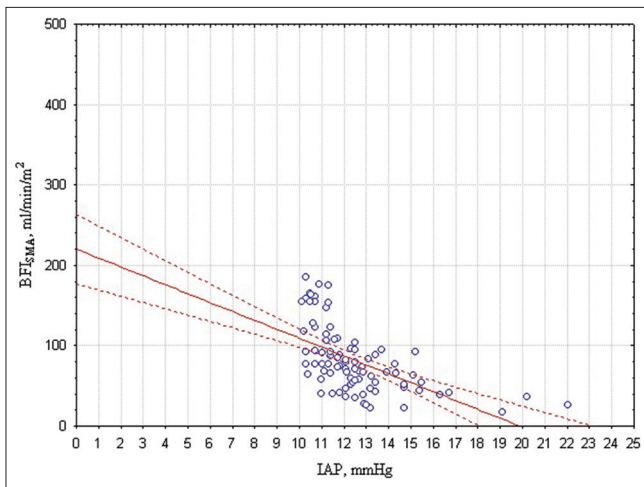
**Table 2: Main study results**

Values/Groups	“without IAH”	“with IAH”	<i>P</i>
IAP, mmHg M±SD	7.63±1.64	12.66±2.22	0.0043
$BF_{SMA}$ , ml/min Me (Q1;Q3)	95.66 (70.95; 204.82)	54.02 (42.44; 92.52)	<0.0001
$BFI_{SMA}$ , ml/min/m <sup>2</sup> Me (Q1;Q3)	137.30 (75.25; 214.03)	74.67 (53.86; 95.15)	<0.0001
$BF_{PV}$ , ml/min Me (Q1;Q3)	406.91 (253.40; 654.59)	221.78 (142.12; 385.51)	<0.0001
$BFI_{PV}$ , ml/min/m <sup>2</sup> Me (Q1;Q3)	377.41 (242.09; 580.24)	238.20 (175.85; 342.96)	<0.0001
MAP, mmHg M±SD	81.97±11.02	78.86±9.29	0.036
APP, mmHg M±SD	71.48±9.61	69.44±11.07	0.17

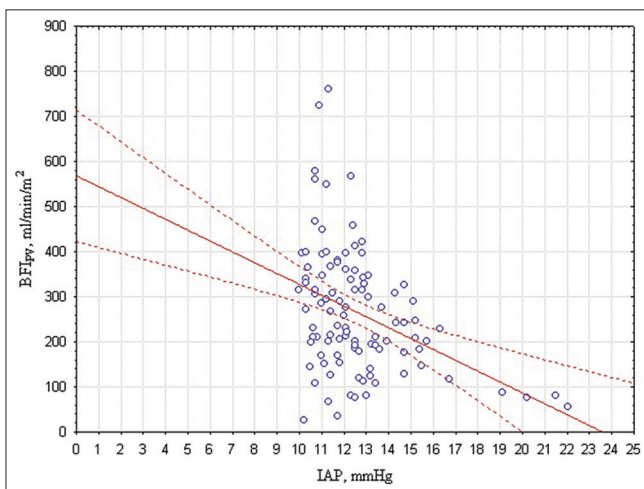
IAH - intraabdominal hypertension; IAP - intra-abdominal pressure;  $BF_{SMA}$  - superior mesenteric artery volumetric blood flow;  $BFI_{SMA}$  - superior mesenteric artery blood flow index;  $BF_{PV}$  - portal vein volumetric blood flow;  $BFI_{PV}$  - portal vein blood flow index; MAP - mean arterial pressure; APP - abdominal perfusion pressure



**Figure 1:** Correlation between IAP and BFISMA in group “without IAH”. IAH - intraabdominal hypertension; IAP - intra-abdominal pressure; BFISMA - superior mesenteric artery blood flow index



**Figure 2:** Correlation between IAP and BFISMA in group “with IAH”. IAH - intraabdominal hypertension; IAP - intra-abdominal pressure; BFISMA - superior mesenteric artery blood flow index



**Figure 3:** Correlation between IAP and BFIPV in group “with IAH”. IAH - intraabdominal hypertension; IAP - intra-abdominal pressure; BFIPV - portal vein blood flow index

Our data confirm the results of above listed experimental studies as we showed a significant reduction in  $BF_{SMA}$  by 54.38% in group “with IAH” compared to group “without IAH”.

In contrast, Ferrara *et al.* have not found differences in  $BF_{SMA}$  between sheep with IAH (20 mm Hg for 2 hours) and sheep with normal IAP.<sup>[13]</sup> This can be attributed to small sample size in Ferrara’s *et al.* study.

In the same way  $BF_{PV}$  impairments in animals with IAH have been shown. In Windberger’s *et al.* study after application of IAP of 14 mm Hg for 30 minutes in 10 healthy pigs  $BF_{PV}$  was decreased compared to baseline.<sup>[14]</sup> Significant changes in  $BF_{PV}$  were observed in anesthetized rats after inflation of air in peritoneal cavity. IAP of 3 mm Hg resulted in a 26% decrease in  $BF_{PV}$  and IAP of 6 mm Hg caused twofold decrease in  $BF_{PV}$  compared to baseline.<sup>[11]</sup> Kotzampassi *et al.* showed that application of IAP of 12 mm Hg in pigs ventilated with positive end-expiratory pressure led to 24% decrease in  $BF_{PV}$ .<sup>[12]</sup> In the study of Schmandra *et al.* pneumoperitoneum with IAP of 8 mm Hg caused reduction in portal blood flow to 38.2% compared to baseline, whereas IAP of 12 mm Hg led to  $BF_{PV}$  reduction to 16% of initial values in rats.<sup>[15]</sup>

In Jakimowicz’s *et al.* study patients, undergoing laparoscopic cholecystectomy had decreased  $BF_{PV}$  during the procedure. At IAP of 7 and 14 mm Hg mean  $BF_{PV}$  was decreased by 37% and 53% respectively compared to baseline.<sup>[16]</sup>

Our results are in line with the results of the abovementioned studies. We have found that  $BF_{PV}$  was decreased significantly in group “with IAH” by 63.11% compared to group “without IAH”.

Unlike this Gudmundsson *et al.* have not found differences of  $BF_{PV}$  before and 3 hours after of 20 mm Hg IAP application in anesthetized pigs. But when IAP was increased to 30 mm Hg, reduction of  $BF_{PV}$  occurred.<sup>[17]</sup> This discrepancy can be explained by short observation period and small sample size in Gudmundsson’s *et al.* study.

Higher MAP in patients in group “with IAH” can be explained by physiologic compensation of splanchnic hypoperfusion by means of increased systemic vascular resistance and activation of the renin-angiotensin-aldosterone system.<sup>[18]</sup>

Diebel *et al.* have found negative correlation between IAP and splanchnic blood flow in experimental studies.<sup>[8]</sup> However, correlation analysis of IAP and splanchnic blood flow measured

directly in clinical setting have not been made before. We found strong negative correlation between IAP and  $BFI_{SMA}$  ( $r_s = -0.66$ ;  $P < 0.0001$ ) and weak negative correlation between IAP and  $BFI_{PV}$  ( $r_s = -0.36$ ;  $P = 0.0001$ ) in group “with IAH”. Weak correlation between IAP and  $BFI_{PV}$  can be explained by the fact, that fluid outflow from splanchnic organs is carried out not only by portal blood flow but by lymphatic system too. It is difficult to assess the extent of lymphatic drainage from the splanchnic organs and its relationships with portal outflow in clinic. So, we consider that  $BFI_{SMA}$  is better tool to assess splanchnic blood flow impairments in patients with IAH. Weak negative correlation between IAP and  $BFI_{SMA}$  ( $r_s = -0.30$ ;  $P = 0.0047$ ) and negligible nonsignificant correlation between IAP and  $BFI_{PV}$  ( $r_s = -0.04$ ;  $P = 0.7$ ) was observed in group “without IAH”. It can be explained by preserved abdominal wall compliance in children of this group, when increase in intraabdominal volume did not reach critical point to cause exponential IAP growth and splanchnic blood flow compromise.

Relationship of splanchnic circulation and APP is not studied well and there are some controversies in APP interpretation in patients with IAH. On the one hand there is scientific evidence that APP can be better predictor of survival than the lowest MAP, the highest IAP, the highest lactate, the highest base deficit and the lowest urine output in surgical and trauma ICU patients with IAH.<sup>[20]</sup> Because of this and because of the correlation between APP and visceral perfusion, earlier APP was used as a resuscitation endpoint in patients with IAH.<sup>[20]</sup> On the other hand, WSACS experts consider that there is not sufficient evidence to recommend APP as a resuscitation endpoint in patients with IAH, besides optimal level of APP in children is not clearly defined.<sup>[5]</sup> Likewise, in another study by Ferrara *et al.* there was no correlation between APP and mesenteric blood flow in sheep with IAH of 20 mm Hg.<sup>[13]</sup> We also did not find statistically significant correlation between APP and  $BFI_{SMA}$  or  $BFI_{PV}$ , so our data confirm Ferrara’s *et al.* study results.

Further investigations on IAH and splanchnic blood flow in children are needed to verify our results.

### Study limitations

Value of the study can be limited by relatively small sample size. Besides, most of children in IAH group had IAP levels in range of 10-15 mm Hg, so it was difficult to assess how higher IAP levels affect splanchnic blood flow.

### Conclusion

Elevated IAP significantly reduces splanchnic blood flow in children with appendicular peritonitis. Superior mesenteric

artery blood flow index and portal vein blood flow index negatively correlate with intraabdominal pressure in these patients. There is no correlation between abdominal perfusion pressure and mesenteric artery blood flow index and portal vein blood flow index in children with IAH due to appendicular peritonitis.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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