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## **Intra-abdominal hypertension as a risk factor for acute kidney injury in geriatric patients after emergency abdominal surgery**

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**Key words:** geriatric patients; acute kidney injury; intra-abdominal hypertension.

## **Abstract**

Intra-abdominal hypertension is an often underestimated risk factor for acute kidney injury (AKI). But the values of intra-abdominal pressure (IAP) and abdominal perfusion pressure (APP), which are critical for the development of AKI in elderly patients after urgent abdominal surgery, are still not defined.

**Objective.** To evaluate the relationship between IAP and APP and the development of acute kidney injury in geriatric patients after emergency abdominal surgery.

**Materials and methods.** A prospective single-center study included 66 patients older than 60 years who underwent surgery for peritonitis and were transferred to the intensive care unit. Statistical processing was performed using the program "STATISTICA for Windows 13" (StatSoftInc., No. JPZ804I382130ARCN10-J).

**Results.** Among the examined patients, 48 developed AKI (73%). The average values of IAP in patients with AKI and without AKI were 10.4 (7.4, 13.3) mm Hg and 6.7 (4.4; 9.6) mm Hg respectively ( $p < 0.0001$ ). APP in patients with AKI, respectively, was significantly lower (72 (61.5, 83.7)) than in patients without AKI (85.6 (74.5, 94.4;  $p < 0.0001$ )). According to the results of logistic regression analysis, a relationship between high IAP values and the development of AKI was revealed: the odds ratio (OR) was 3.4 with the value of the criterion  $\chi^2 = 32.4$  ( $p < 0.0001$ ). The odds ratio between the reduction of APP and the development of AKI was 2.3 with the value of the criterion  $\chi^2 = 13.4$  ( $p = 0.0002$ ). ROC analysis showed that  $IAP > 10.4$  mm Hg. is the threshold level for the development of AKI with a sensitivity of 46% and a specificity of 90.5%, with an area under the AUC curve of 0.74 ( $p < 0.001$ ).  $APP < 79.12$  mm Hg is critical for the development of AKI, with a sensitivity of 66.4% and a specificity of 70%, with an area under the AUC curve of 0.68 ( $p < 0.001$ ).

**Conclusions.** High values of IAP and reduction of APP are associated with the occurrence of acute kidney injury in elderly patients after emergency abdominal surgery.

**Introduction.** Due to the rapid development of the health care system, the quality of medical care and disease prevention, the number of surgical patients in the elderly is increasing significantly [1]. Geriatric patients account for about 25% of patients admitted to emergency departments with abdominal pain [2-4]. They are characterised by a decline in physiological reserves, age-related anatomical and functional changes in organs, a high level of comorbidities and, as a result, drug polypharmacy [5, 6]. These factors increase the risk of complications in the postoperative period, one of which is acute kidney injury (AKI) [7].

Intra-abdominal hypertension (IAH) is an important pathophysiological mechanism of AKI [8]. This can affect kidney function both indirectly through the cardiovascular system and directly lead to impaired renal blood flow due to vasoconstriction and local increase in vascular resistance. The mechanism of systemic effects of IAH is realised through an increase in intrathoracic pressure, a decrease in cardiac preload and cardiac output, which leads to a decrease in glomerular filtration rate both due to arterial hypoperfusion of the kidneys and venous stasis in them. In experimental conditions, it has been shown that when intra-abdominal pressure (IAP) increases to 20 mm Hg, the directly measured pressure in the renal vein can increase from 5.8 mm Hg to 18.3 mm Hg, and urine flow can decrease by half of the normal value [9, 10].

According to the consensus of the World Society for Abdominal Compartment Syndrome, IAP is defined as a persistent pathological increase in IAP  $\geq 12$  mm Hg [11]. For geriatric patients, the values of IAP and abdominal perfusion pressure (APP), which are critical for the development of postoperative AKI, may differ from those generally known.

**The aim of the study** was to evaluate the relationship between IAP and APP and the occurrence of AKI in geriatric patients after emergency abdominal surgery.

**Materials and methods.** After passing the Bioethics Committee at Zaporizhzhia State Medical and Pharmaceutical University and obtaining informed consent, 71 patients over 60 years of age who had undergone emergency surgery for peritonitis and were admitted to the intensive care unit (ICU) for postoperative treatment were consecutively included in a single-centre prospective study. Exclusion criteria were: urine bladder damage, history of chronic renal failure (CRF), peritonitis due to severe pancreatitis or pancreatic necrosis, and ICU admission after relaparotomy.

Perioperatively, patients underwent standard monitoring, additionally determining the risk of developing AKI using the ACS-NSQIP calculator [12], the severity of the patients' condition using the SOFA scale [13], cardiac index (CI) using esCOO technology (Vismo

PVM-2701K monitor, Nihon Kohden, Japan), the presence and stage of AKI according to the KDIGO classification [14].

Intra-abdominal pressure (IAP) was determined by the indirect transvesical method (Kron and Iberti, 1984), which consists of injecting 50 ml of saline through the urinary catheter into the bladder and determining the level of the fluid column (H<sub>2</sub> O) in the infusion system in centimetres. The value of IAP in cm H<sub>2</sub> O was converted to mm Hg using the following equation: 1 cm H<sub>2</sub> O = 0.74 mm Hg. The IAP was measured daily, in the morning, simultaneously with haemodynamic monitoring, for 7 days. Abdominal perfusion pressure (APP) was defined as the difference between mean arterial pressure and IAP.

Statistical analyses were performed using STATISTICA for Windows 13 (StatSoftInc., No. JPZ804I382130ARCN10-J). The results of continuous variables were described using medians and interquartile ranges. Categorical data are presented as percentages. The Mann-Whitney U test was used to compare the clinical characteristics of patients with and without AKI. Spearman's coefficient and Gamma coefficient were used to determine the correlation between the variables. ROC analysis was used to investigate the relationship between IAP, APP and AKI. Differences with a p-value of <0.05 were considered significant.

**Results of the study.** Of the 71 patients initially included in the study, 5 patients were excluded due to the presence of pancreatic necrosis (n=2) or a history of chronic kidney disease (CKD) (n=2), and due to the technical impossibility of transvesical IAP measurement (n=1). 66 patients were included in the final analysis, the characteristics of which are presented in Table 1 (indicators are determined both for all patients and separately for patients with and without AKI).

**Table 1:** General characteristics of patients and risk factors for AKI

Characteristic	All patients (n=66)	AKI (n=48)	No AKI(n=18)	P
Age, years	75 (67; 81)	74 (67,5; 80,5)	81 (65; 82)	0,21
Male gender, n (%)	27 (41%)	17 (36,2%)	10 (52,6%)	0,21
BMI, kg/m <sup>2</sup>	24,9 (22,6; 31,1)	25,7 (23,4; 31,2)	22,85 (21,6; 27,7)	0,09
<b>Comorbid pathology</b>				
Heart failure, n (%)	45 (68%)	32 (66,7%)	13 (72%)	0,74
Hypertension, n (%)	58 (87,9%)	43 (89,6%)	15 (83,3%)	0,7
Diabetes mellitus, n (%)	13 (19,7%)	12 (25%)	1 (5,6%)	0,23
<b>Preoperative period</b>				
ASA, class	3 (3; 4)	3 (3; 4)	3 (3; 3)	0,19
Risk of AKI, %.	4,9 (2,1; 7,8)	5,25 (2,55; 8,8)	3,1 (0,8; 4,9)	0,03
Baseline Hb, g/l	125 (96; 149)	126,5 (98; 151)	119 (95; 147)	0,75
Anaemia, n (%)	22 (33,3%)	16 (33,3%)	6 (33,3%)	0,97
<b>Intraoperative period</b>				
Operation:				
Laparotomy, n (%)	62 (94%)	46 (95,8%)	16 (88,9%)	0,067
Laparoscopy, n (%)	4 (6%)	2 (4,2%)	2 (11,1%)	0,067
Operation duration, min	115 (80; 150)	120 (90; 160)	90 (75; 110)	0,037
Duration of anaesthesia, min	130 (95; 177,5)	135 (110; 197,5)	102,5 (80; 127,5)	0,04
Total fluid infusion, ml	2200 (1300; 3200)	2300 (1300; 3200)	1900 (1200; 3200)	0,46
Sympathomimetic drug, n (%)	27 (41%)	22 (45,8%)	5 (27,8%)	0,34
<b>Postoperative period</b>				
SOFA, points	3 (2; 4)	3 (2; 4,5)	3 (2; 3)	0,21
Anaemia, n (%)	42 (63,6%)	33 (68,75%)	9 (50,0%)	0,25
Fluid infusion, ml/day	2400 (1800; 3050)	2400 (1800; 2900)	2375 (2050; 3100)	0,72

Sympathomimetic drug, n (%)	31 (47%)	26 (54,2%)	5 (27,8%)	0,1
Hemotransfusion, n (%)	15 (22,7%)	12 (25%)	3 (16,7%)	0,6
CI, l/min-m <sup>2</sup>	3,26 (2,74; 4,01)	3,25 (2,68; 3,96)	3,28 (2,95; 4,12)	0,28
MAP, mm Hg	87 (73; 97)	84 (72; 95)	93 (82; 103)	0,005
IAP, mm Hg	9 (6; 12)	10,4 (7,4; 13,3)	6,7 (4,4; 9,6)	<0,0001
APP, mm Hg	77 (64; 88,6)	72 (61,5; 83,7)	85,6 (74,5; 94,4)	<0,0001
IAH (IAP>12 mm Hg), n (%)	22 (33%)	22 (46%)	0	0,004

Notes: BMI - body mass index; CI - cardiac index; MAP - mean arterial pressure; IAP - intra-abdominal pressure; APP - abdominal perfusion pressure; IAH - intra-abdominal hypertension.

As shown in Table 1, the groups of patients were comparable in terms of age, gender, body mass index. 48 patients (73%) developed AKI in the postoperative period. According to the ASC-NSQIP calculator, patients with AKI had a 1.7-fold significantly higher risk of AKI ( $p=0.03$ ), as well as a longer surgical intervention ( $p=0.037$ ) and, as a result, anaesthesia time ( $p=0.04$ ). During perioperativ period, patients with AKI had an average MAP level 10% lower than patients without AKI ( $p=0.005$ ), but the cardiac index values did not differ significantly between the groups ( $p=0.28$ ). This was probably due to the use of sympathomimetics, because despite the significant difference, MAP was sufficient in both groups (84 (72; 95) mm Hg in patients with AKI and 93 (82; 103) mm Hg in patients without AKI).

Patients who developed AKI had an average of 3.7 mm Hg higher IAP ( $p<0.0001$ ) and significantly lower APP( $p<0.0001$ ). However, it is interesting that none of the patients without AKI had intra-abdominal hypertension, while in patients with AKI it occurred in 46% of cases. The above-mentioned determined the further definition: Was the IAH a predictor of more severe AKI, and the normal level of IAP a predictor of renal function recovery in elderly patients after abdominal surgery? These data are presented in Table 2.

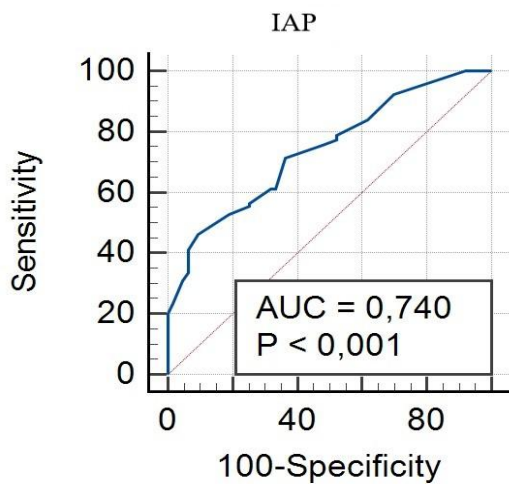
**Table 2.** Dependence of the stage of AKI on the presence/absence of IAH

Indicator.	All patients (n=66)	IAH (n=22)	Without IAH (n=44)	p
AKI, n (%)	48 (73%)	22 (100%)	26 (59%)	0,007
AKI, Stage 1, n (%)	27 (56%)	11 (50%)	16 (62%)	0,5
AKI, Stage 2, n (%)	10 (21%)	5 (23%)	5 (19%)	0,8
AKI, Stage 3, n (%)	11 (23%)	6 (27%)	5 (19%)	0,6
Renal function recovery, n (%)	31 (65%)	11 (50%)	20 (77%)	0,056

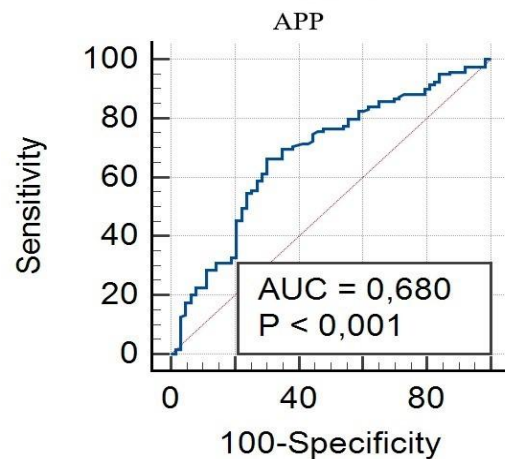
As can be seen from Table 2, patients with intra-abdominal hypertension had a significantly higher frequency of AKI ( $p=0.007$ ), but IAH had no effect on the severity of renal dysfunction or on the subsequent recovery of renal function.

The results of logistic regression analysis revealed a relationship between high IAP values and the development of AKI: the odds ratio (OR) was 3.4 with a value of criterion  $\chi^2 = 32.4$  ( $p=0.0000$ ). The risk of developing AKI was also significantly increased in patients with reduced APP (OR 2.3;  $\chi^2 = 13.4$ ;  $p=0.0002$ ).

ROC analysis showed that IAP >10.4 mm Hg is a threshold level for the development of AKI with a low sensitivity of 46% but high specificity of 90.5% (area under the AUC curve 0.74 ( $p<0.001$ )) (Fig. 1). It was determined that the value of APP <79.12 mm Hg is critical for the development of AKI, with almost the same sensitivity (66.4%) and specificity (70%) (area under the AUC curve 0.68 ( $p<0.001$ )) (Fig. 2).



**Fig. 1.** ROC curve of the IAP value



**Fig. 2.** ROC curve of the APP value

**Discussion:** Acute kidney injury in the postoperative period is a common problem, especially in intensive care units. According to various authors, the incidence of AKI in critically ill patients varies from 31.6% to 67% [15-18], and leads to longer hospitalisation, increased risk of progression to chronic kidney disease, and increased short- and long-term mortality [19-22]. There is a lot of evidence in the literature that clearly demonstrates the association between intra-abdominal hypertension and renal dysfunction in the general population [9, 23-26]. A meta-analysis by Sun J. et al. showed that IAH increases the risk of AKI regardless of the average age ( $\geq 60$  years: OR=2.56, 95% CI (1.16-5.63),  $p=0.02$ ;  $<60$  years: OR=2.57, 95% CI (1.33-4.98),  $p=0.005$ ) [27]. According to our previous study, which included only geriatric patients, patients with AKI perioperatively had an average of 4 mm Hg higher IAP compared with patients without AKI ( $p=0.005$ ), and their level of APP was significantly lower (64 (54; 80.7) mm Hg vs. 82.2 (65.8; 112.1) mm Hg, respectively,  $p=0.0348$ ) [28].

Despite the large evidence base for the effect of IAP/APP on the development of AKI, several questions remain open. Firstly, is intra-abdominal hypertension primary in the development of renal dysfunction? According to Chang H.J. and colleagues, the absence of IAH in 57 patients with AKI did not predict recovery of renal function and did not affect in-hospital mortality [29]. Our study demonstrated that despite a significantly higher incidence of AKI in patients with IAH, there was no difference between the severity of renal dysfunction and recovery of renal function. Based on these results, we cannot conclude which is the primary, AKI or IAH, but there is no doubt that IAH is a risk factor for AKI.

Jung Eun Lee et al. suggested that IAH is a secondary phenomenon after the



development of AKI[8]. In such conditions, IAH may increase due to fluid retention in the body during infusion therapy. In addition, a meta-analysis by Malbrain M.L. and colleagues [30], which analysed the results of treatment of 19902 patients, showed that after one week in the intensive care unit (ICU), patients with IAH had a more positive cumulative fluid balance (+3.4 litres). Interventions aimed at reducing fluid balance led to a decrease in IAP: an average weekly total fluid removal of 4.9 litres led to a decrease in IAP from  $19.3 \pm 9.1$  mm Hg to  $11.5 \pm 3.9$  mm Hg. The authors concluded that a positive cumulative fluid balance contributes to the development of IAH and worsens treatment outcomes, even in patients without primary AKI.

The second controversial issue concerns the anatomical and physiological features of elderly patients and their impact on the critical values of IAP in this category of patients, which are crucial for the development of AKI. According to many authors, the incidence of IAH in critically ill ICU patients is approximately 34-43% [31-34], and in some cases reaches 78.9% [29]. The frequency of IAH in our study was 33%. This rate is even lower than in the general patient population, which does not coincide with the data of the study by Dalfino L. et al [35], who identified age as an independent prognostic factor for IAH. In addition, the above-mentioned authors determined the cut-off point of IAH for the development of AKI to be 12 mm Hg (sensitivity 91.3%, specificity 67%), and the threshold value of APP to be 52 mm Hg (AUC 0.825; SE 0.058; 99% CI 0.68-0.97;  $p < 0.0001$ ). According to the results of our study, the threshold value of IAP critical for the development of AKI is slightly lower (IAP  $> 10.4$  mm Hg, sensitivity 46%, specificity 90.5%, AUC 0.74;  $p < 0.001$ ), and the APP is slightly higher (APP  $< 79.12$  mm Hg, sensitivity 66.4%, specificity 70%, AUC 0.68;  $p < 0.001$ ). Such discrepancies in the values of IAP and APP in relation to the development of AKI in geriatric patients are interesting and require further study in more homogeneous groups of patients.

**Conclusions:** High IAP and decreased APP are associated with acute kidney injury in geriatric patients after emergency abdominal surgery. The critical values of IAP and APP in geriatric patients for the onset of renal dysfunction are probably different from those in the general population and are as follows: IAP  $> 10.4$  mm Hg, APP  $< 79.12$  mm Hg. IAP is a less sensitive but more specific marker of the development of AKI than APP.

**Prospects for further research:** This study showed that IAH was associated with a higher prevalence of AKI. Further studies are needed to verify the relationship between IAH and AKI in geriatric patients, as a particularly vulnerable group, and to determine how IAH-induced acute kidney injury can be prevented.

Nataliia Momot: conceptualization, methodology, investigation, formal analysis, writing - rough preparation, writing - review and editing, visualization.

Sergiy Vorotyntsev: conceptualization, check, writing - review and editing, visualization, supervision.

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The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the the Bioethics Commission of the Zaporizhzhia State Medical and Pharmaceutical University (protocol code10, from 01.10.2019 )

Informed consent was obtained from all subjects involved in the study.

Conflicts of interest: authors have no conflict of interest to declare.

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