Clinical Effects and Prognostic Significance of Intraabdominal Pressure in Secondary Peritonitis

Dafina Mahmutaj¹, Bedri Braha¹*, Astrit Hamza², Jehona Krasniqi²

1. Surgery Clinic, University Clinical Center of Kosova, Prishtina, Kosovo.
2. Faculty of Medicine, University of Prishtina "Hasan Prishtina", Prishtina, Kosovo.
3. College of Medical Science “Rezonanca”, Prishtina, Kosovo.

Abstract
The aim of this study was to determine the role of IAH degrees in disease progression and the impact on mortality rate in patients operated for secondary peritonitis.

IAP measurements via the urinary bladder were conducted in 112 patients before and after operations three times over 24 h. Based on IAP values, three patient groups were established: Gr-I: IAP 12–15 mmHg, Gr-II: IAP 16–20 mmHg and Gr-III and IV > 20 mmHg (single group). Intra-abdominal hypertension (IAH) was observed in 82 patients (74.1%); 57.5% had IAH Gr-I, Gr-II had 30.0%, and Gr-III and Gr-IV had 12.5%. Abdominal perfusion pressure (APP) and filtration gradient (FG) before surgery were significantly different, according to IAH groups. After surgery, APP differences according to IAH groups remained significant, while we observed no significant postoperative differences in FG according to IAH groups. Before and after operations, we observed no differences between white blood cell (WBC) counts and body mass indices (BMI) amongst groups. Our study showed a significant statistical difference between groups of IAH for mean arterial pressure (MAP), urine output and fluid balance, creatinine, C-reactive protein (CRP), procalcitonin (PCT), acute physiology and chronic health evaluation II (APACHE II) mortality, sequential organ failure assessment (SOFA) mortality, multiple organ dysfunction score (MODS) mortality, index Mannheim peritonitis (IMP) mortality, and CT ratio of anteroposterior to transverse abdominal diameter (CT diameter: AP/T). Groups of APP: Gr-I APP > 60 mmHg and Gr-II APP < 60 mmHg showed a significant difference for several variables, including MAP, urine output and fluid balance, creatinine, CRP, PCT, APACHE II, SOFA, MODS and IMP mortality, FG, APP and CT diameter: AP/T. For WBC counts in groups, we observed no significant differences.

Measuring IAP and determination of the degrees of IAH and values of APP were of great importance for the placement of further steps for the treatment of patients with secondary peritonitis.

Keywords: Intra-abdominal pressure, intra-abdominal hypertension degrees, abdominal perfusion pressure, secondary peritonitis.

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Introduction
Increased pressure within the abdominal space is likely to occur in all cases where risk factors were present. Cases operated on as abdominal emergencies with the presence of secondary peritonitis were more likely to increase intraabdominal pressure (IAP) than other cases, especially when considering elective cases.¹ The appearance of IAH is common in bacterial peritonitis, and in cases where the disease advanced, the manifestation of IAH becomes more frequent, contributing to the appearance of changes in the organs and an increase in mortality.²,³,⁴,⁵,⁶,⁷ The measurement of the IAP and the determination of its normal values have been the subject of study and has led to the establishment of recommendations by World Society of the Abdominal Compartment Syndrome (WSACS; http://www.wsacs.org) regarding the normal values of the IAP and the values indicating for HIA. If the value of IAP is higher than 12 mmHg it is considered as IAH while the normal value of IAP is taken the value <5-7mmHg.⁸,⁹,¹⁰
In patients operated on due to secondary peritonitis, it is important to measure IAP and monitor arterial pressure. From measured arterial pressure is calculated MAP (Mean Arterial Pressure). Based on the values of these parameters we can determine the perfusion in the abdominal tissues, of particular importance is the blood circulation in the kidneys. APP calculation is done when we subtract the IAP values from the MAP values (APP = MAP - IAP). To maintain proper blood circulation in the abdominal organs, we must keep the APP above 60 mmHg, due to the importance of tissue perfusion in proper course of the disease in patients with HIA and CSA (Compartment Abdominal Syndrome). 

This study aimed to analyze the role of IAH in secondary peritonitis, the association of IAH degrees with the stage of the disease. We have also claimed to determine whether IAH degrees have been associated with parameters that indicate intraabdominal tissue perfusion, and correlation with infection biomarkers, mortality rate scores, and other important parameters that predict outcome and mortality. The same variables were analyzed in relation to APP to determine its role in the treatment and progression of the disease.

**Materials and methods**

The research involved 108 patient’s hospitalized as emergency abdominal cases with secondary peritonitis, diagnosed and treated at the Emergency, Clinic of Surgery and Intensive Care at University Clinical Centre of Kosovo, in Prishtina between May 2018 and July 2019. The study was conducted on the basis of protocol approved by the Ethics Committee of the Faculty of Medicine at the University of Prishtina. This was a prospective, clinical, and observational study. Inclusion criteria were: aged > 18 years, both genders, patients operated on as an emergency cases with presence of peritonitis. Exclusive criteria included: urethral injuries, immunosuppression, chronic renal failure, liver cirrhosis, acute hepatic insufficiency, diabetes and long-term corticosteroid use.

In this study, the basic criterion was the measurement of preoperative IAH, where it was evaluated as IAH according to guidelines of WSACS. The measurements were performed before operation and after surgery three times over 24 h, and averaged daily. Measurements continued until IAP normalization.

The measurement was performed using the modified Kron technique. We have used the guidelines from WACS to determined APP (APP = MAP - IAP) and filtration gradient (FG) (FG = MAP - 2 x IAP). A mean APP < 60 mmHg was considered abnormal. The ratio of the anteroposterior abdominal diameter to the lateral diameter was defined, if ACS (abdominal compartment syndrome) was present, as higher than 0.8. In our study the CT diameter AP/T and ratios between them were measured before the operation. Based on the weight of patients, diuresis within 24 h and the amount of fluid normalized at this time, urine outputs and fluid balances were determined using Urine Output and Fluid Balance MD Calc. by creator Dr Saulo Klahr (normal output for adult patients = 0.5–1cc/kg/h).

We also collected many parameters especially those that we needed for calculating mortality severity scores: age, gender, body mass index (BMI), APACHE II (acute physiology and chronic health evaluation II), SOFA (sequential organ failure assessment), MODS (multiple organ dysfunction score) and IMP (index Mannheim peritonitis) score, admission hemoglobin, albumin, creatinine, bilirubin, gas analysis, electrolytes, platelets, CRP (C reactive protein), WBC (white blood cell), PCT (procalcitonin), the ratio of partial arterial oxygen pressure to fraction inspired oxygen (PaO2/FiO2) and CVP (central venous pressure). Based on IAP values, three patient groups were established: Gr-I: IAP 12–15 mmHg, Gr-II: IAP 16–20 mmHg and Gr-III and IV > 20 mmHg (single group).

**Statistical analysis**

Data were analyzed using SPSS software version 18.0 (Chicago, IL, USA). Descriptive statistics, means and measures of variability (standard deviation), minimum and maximum values were used to describe numerical characteristics. For homogenous data we used Pearson's correlation coefficient and for non-homogeneous data Spearman’s correlation coefficient. We used the Kruskal Wallis and ANOVA test for demographic variables, which were compared between different IAP groups. Testing of qualitative data with normal distribution was performed using T test and One Way ANOVA . The Mann-Whitney test was used for...
independent samples. The difference between the parameters before and after the surgery was analyzed using Wilkoxon test. Significant differences were accepted at P < 0.05.

Results

This study included 112 surgical patients with secondary peritonitis, of which 39 were female and 73 were male. The mean age was 43.7 years (SD ± 19.2 years). Of the 112 patients, 22 (25.9%) had IAP < 12 mmHg, while 82 (74.1%) had IAP ≥ 12 mmHg, therefore the IAH incidence was 74.1%. The mean age of patients with IAH was 49.4 years (SD ± 18.3 years), whereas in group of patients without IAH the mean age was 27.6 years (SD ± 10.5 years).

Using the Mann-Whitney test, we didn’t find significant statistical differences between groups in the mean ages (P = 0.000). Of the 80 patients with IAH in the Gr-I were included 57.5%, Gr-II had 30.0%, and Gr-III-IV had 12.5%. The mean age of patients in Gr-I with IAH was 43.3 years (SD ± 17.5 years), those in Gr-II with IAH, 57.3 years (SD ± 17.5 years), and those with IAH in Gr-III and IV was (SD ± 14.5 years). Using the Kruskal Wallis test, we observed statistically significant differences between the average age by group. IAH Gr-III occurred in 43.75% of cases with severe sepsis, and in 50% of cases with septic shock, IAH Gr-II was present in 25% of cases with severe sepsis and in 33% of cases with septic shock. But in our analysis we have IAH Gr-I in 31.25% of cases with severe sepsis and in 16.6% of cases with septic shock.

APP and FG conducted before surgery were significantly different according to IAH groups. After surgery, the difference between APP according to IAH degrees remained significant, while we observed no significant postoperative differences for FG, according to IAH degrees. Difference in FG before and after surgical decompression were significant (51.4 ± 17.9 before operation, 58.6 ± 16.2 post-operation, P = 0.009). For APP, we observed significant improvements after surgical decompression (66.6 ± 17.0 before operation, 71.7 ± 14.4 post-operation, T = 3.58, P = 0.0006). Before operation, white blood cell (WBC) counts among groups were not significantly different, but postoperatively, statistical differences between groups in WBC were significant. According to IAH groups there was no statistical differences in BMI. We also observed significant differences between groups for MAP, urine output and fluid balance, creatinine, CRP, PCT, APACHE II, SOFA, MODS and IMP mortality, and CT diameter: AP/T. (Table 1).

Mortality in patients operated on for secondary peritonitis with IAH was 12.3%, in contrast to the groups, mortality in IAH Gr-I was 2.1%, in IAH Gr-II was 23% while in IAH Gr-III-IV mortality was quite high 83.3%.

APP and FG analyses in IAH groups revealed minimal values in patients with high IAP-Gr-II and G-III values. The correlation of IAH Gr. III-IV with BMI was moderate. In IAH Gr-I, we observed no correlations with APP, FG and creatinine (Table 2).

We analyzed correlations between IAP and hospital mortality in patients with secondary peritonitis as determined by the predictive scoring systems. Spearman’s analyses showed moderate significant positive correlations of IAH with mortality defined by APACHE II ( r=0,56, P<0.001), IMP (r=0.55, P<0.0001), SOFA(r=0.49, P<0.0001) and MODS (r=0.47, P<0.0001) (Figure 1). Between two groups of APP: Gr-I APP > 60 mmHg and Gr-II APP < 60 mmHg, statistical difference was significant for several variables, including, MAP, urine output and fluid balance, creatinine, CRP, PCT, APACHE II, SOFA, MODS and IMP mortality, FG, APP and CT diameter: AP/T. For WBC counts and BMI amongst these groups of APP, no significant differences were observed (Table 3).

FG analyses revealed minimum values with minimum APP <60mmHg, also these patients had minimum MAP values, but high IAP, creatinine and PCT values (Table 4).

Discussion

Our study demonstrated a high incidence of IAH (74.1 %) in surgical patients, operated on for secondary peritonitis. This IAH incidence is however, not comparable with the literature. Arabadzhiev observed that IAH prevalence in patients undergoing emergency surgery was 43.37% . Muturi et al. noted a prevalence of IAH and ACS of 67.3% in intensive care units (ICU) patients. A possible explanation for the high incidence of IAH in our study could be that all patients included in our study had free intra-peritoneal fluid and abdominal packs distended, associated with visceral edema. Also, aggressive
fluid restitution before and after operations contributed to IAH appearance.

Abdominal sepsis was present in all patients, in some cases it progressed to severe sepsis and septic shock. GIII and IV of IAH were present in severe sepsis and septic shock, however we had cases with low IAP but very worst outcomes (31.25% Gr-I of IAH in severe sepsis). Data from Maddison suggested that microcirculation and tissue perfusion undergoes changes during IAH Gr-I and Gr-II. 17 Studies by other authors concluded that organ dysfunction and mortality were present in the low grades of IAH and therefore may be considered as a predictive factor.18,19

In contrast, Petro et al. showed that in the operation performed for ventral hernia, IAH Gr-I and Gr-II were present in postoperative period, but they didn't find negative effects of IAH on organ function and disease prognosis 20. According to other authors, mean IAP values were high in patients with organ system dysfunction, when compared to those without this pathology.21, 22, 23

The analyses carried out regarding the grades of IAH and the mortality rate scores in our study found a significant difference between the grades of IAH and the mortality percentage determined by the scores of MODS, SOFA, IMP and APACHE II. Malbrain concluded that Sepsis-Related Organ Failure Assessment scores during the intensive care unit stay were significantly higher than in patients without intraabdominal hypertension. Other studies also showed poor outcomes in patients with IAH 24, 25. According to Habli et al, patients with IAH and worse outcomes had higher scores of APACHE II, APACHE III and SOFA, compared with survival group.26 Another study observed that severely ill patients had high SOFA scores, high IAP that led to organ dysfunction .27

We observed no correlations between MAP and IAH Gr-I and Gr-II, but a positive correlation was observed between IAH GIII-IV and MAP. Decrease in MAP were followed with changes in organ functions especially in kidneys because of the low APP and FG. Svorcan observed that increase of IAP more than 25 mm Hg led to decrease in arterial pressure and poor prognosis .28 We demonstrated that Gr III-IV of IAH showed a decrease in urine outcomes and fluid balance that led to oliguria and 30% of patients had anuria and underwent dialysis. Mullens et al. showed that kidneys and FG were affected when IAH was high (for FG: 56 versus 65 mm Hg, P = 0.03).29 Sugrue et al. reported dysfunction of kidneys when IAH persisted more than 2.7 days end was higher than 25 mmHg. 30

We also demonstrated that low values of MAP followed with high grades of IAH are associated with decrease in APP. These decreased values of APP led to changes in kidney perfusion and urine output and high creatinine levels. Meanwhile values of PCT had strong negative correlation with APP. Similar data were observed by Kovač et al; they observed negative correlations of APP with SIRS, MODS and APACHE II scores.31

Analyzing parameters in two groups: Gr-I APP > 60 mmHg and Gr-II APP < 60 mmHg we found that there is a significant statistical difference between these groups in MAP, urine output and fluid balance, creatinine, CRP, PCT, FG, IAP, and percentage of mortality rate scores, but changes on APP had no impact on WBC values. Meanwhile CT diameter:AP/T and BMI doesn't affect APP. In our study, high IAP and presence of ACS were correlated with low APP. Similar data were observed in other studies.32,33

In a study by Gül, the best threshold for predicting renal dysfunction was an APP value ≤ 72 mmHg. According to this study, APP was superior to IAP in detecting changes in renal perfusion in patients with severe illness. 34

We found that BMI didn’t have statistical difference between IAH groups. Other studies have shown that BMI had significant positive correlations with IAP, and that a BMI ≥ 30 was a risk factor for IAH.35,36

The presence of peritonitis on the researched patient’s caused changes in the value of infection markers such as PCT and CRP. Based on the data from our study we concluded that high IAP degrees correspond with increase in PCT and CRP values. Surgical decompression significantly improved the values of these biomarkers in IAH Gr-I however values of CRP and PCT remained high even after the decompression. According to Raghavendra et al markers such CRP and PCT when correlate with IAP grades showed a significant linear trend (P < 0.05).37

We demonstrated significant differences between groups of IAH for CT diameter: AP/T. According to IAH groups CT diameter: AP/T and Gr I of IAH had a moderate positive correlation.
Patel et al. concluded that CT ratio of anteroposterior diameter and lateral diameter was lower than 0.7, even though these patients had the presence of ACS.36

Our study showed that mortality rates in IAH patients operated on for secondary peritonitis, was 12.3%. Mortality rate was determined with APACHE II, SOFA, MODS and IMP scores. Patients with worse outcome had very low MAP, high IAP, low APP and FG. Keskinen et al. showed that increased lethality was followed with high APACH II scores and increased creatinine and lactate levels.39

Our study design had several limitations in its building and development. It was a case controlled study with a low incidence of severity ill patients aimed to be presented, also predictive parameters showed positive outcomes because of the small sample size of the patients with a higher degree of IAH. Based in the results of our study and review of literature, the degree of IAH is an important indicator to be considered in further establishment of research projects, treatment protocols procedures, respectively operative procedures. "It is necessary to establish a multi-centered research in order to compare the outcome of patients from different regions with different degrees of IAH and to develop a treatment guidelines."

**Conclusions**

Finally, we observed that Gr-III-IV were associated with worse outcomes. If IAH of these degrees persisted, than this led to organ dysfunction with high risk of mortality. Early detection measures to prevent further increases in IAP are important. In the group of patients with APP< 60 mmHg, we had low FG, low urine output and fluid balance, meanwhile creatinine, PCT, CRP were high and they correlated with high mortality defined from APACHE II, MODS, SOFA, and IMP scores.

**Declaration of Interest**

The authors report no conflict of interest.

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### Table 1. Clinical parameters of IAH patients operated on for secondary peritonitis.

*Kruskal-Wallis,* One-way ANOVA, , P-level of significance.
### Table 2. Correlation of IAH grades with test variables.

<table>
<thead>
<tr>
<th>Test Variable</th>
<th>MAP</th>
<th>APP</th>
<th>FG</th>
<th>BMI</th>
<th>Urine outcome and fluid balance</th>
<th>Creatinin</th>
<th>CRP</th>
<th>WBC</th>
<th>PCT</th>
<th>CT-diameter: A-P/T</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Gr-I</td>
<td>Gr-II</td>
<td>Gr-III-IV</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>R</td>
<td>P</td>
<td>R</td>
<td>P</td>
<td></td>
<td>R</td>
<td>P</td>
<td>R</td>
<td>P</td>
<td></td>
</tr>
<tr>
<td>MAP</td>
<td>0.033s</td>
<td>0.90</td>
<td>-0.16s</td>
<td>0.47</td>
<td>0.053s</td>
<td>0.78</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>APP</td>
<td>-0.019s</td>
<td>0.90</td>
<td>-0.46p</td>
<td>0.018</td>
<td>-0.56p</td>
<td>0.057</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FG</td>
<td>-0.091s</td>
<td>0.57</td>
<td>-0.60p</td>
<td>0.001</td>
<td>-0.72s</td>
<td>0.008</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>-0.30s</td>
<td>0.064</td>
<td>-0.14p</td>
<td>0.52</td>
<td>0.42s</td>
<td>0.19</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urine outcome and fluid balance</td>
<td>0.10s</td>
<td>0.50</td>
<td>-0.096s</td>
<td>0.64</td>
<td>0.039s</td>
<td>0.90</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 3: Clinical parameters of patients with secondary peritonitis, according to APP values.

<table>
<thead>
<tr>
<th>Test Variable</th>
<th>APP&gt;60mmHg</th>
<th>APP&lt;60mmHg</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>26.11±4.1</td>
<td>26.95±4.3</td>
<td>0.36a</td>
</tr>
<tr>
<td>MAP</td>
<td>87.56±11.8</td>
<td>66.23±9.6</td>
<td>0.0001b</td>
</tr>
<tr>
<td>Urine outcome and fluid balance</td>
<td>1.02±0.36</td>
<td>0.82±0.54</td>
<td>0.049b</td>
</tr>
<tr>
<td>Creatinine</td>
<td>98±45.31</td>
<td>223.9±196.7</td>
<td>0.001a</td>
</tr>
<tr>
<td>WBC</td>
<td>34.18±17.1</td>
<td>16.11±8.7</td>
<td>0.60b</td>
</tr>
<tr>
<td>PCT</td>
<td>2.5±4.5</td>
<td>22.95±36.42</td>
<td>0.0001a</td>
</tr>
<tr>
<td>CRP</td>
<td>110±82</td>
<td>183.60±97.7</td>
<td>0.0001a</td>
</tr>
<tr>
<td>MODS-mortality (%)</td>
<td>4.1±4.2</td>
<td>29.86±28.86</td>
<td>0.0001a</td>
</tr>
<tr>
<td>APACHE II-mortality (%)</td>
<td>5.9±8.7</td>
<td>39.42±34.25</td>
<td>0.0001a</td>
</tr>
<tr>
<td>SOFA-mortality (%)</td>
<td>10.86±15.7</td>
<td>41.18±32.01</td>
<td>0.0001a</td>
</tr>
<tr>
<td>FG</td>
<td>62.73±9.6</td>
<td>30.91±12.07</td>
<td>0.001b</td>
</tr>
<tr>
<td>IAP</td>
<td>9.6±3.8</td>
<td>16.7±4.9</td>
<td>0.004b</td>
</tr>
<tr>
<td>CT diameter: A-P/T</td>
<td>0.85±0.13</td>
<td>0.87±0.07</td>
<td>0.47a</td>
</tr>
</tbody>
</table>
Prognostic Significance of Intraabdominal Pressure

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Table 4. APP correlations with test variables, before and after operations.
R - correlation coefficient, P - level of significance.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Before operation</th>
<th>After operation</th>
</tr>
</thead>
<tbody>
<tr>
<td>IAP</td>
<td>-0.56</td>
<td>-0.53</td>
</tr>
<tr>
<td>FG</td>
<td>0.98</td>
<td>0.92</td>
</tr>
<tr>
<td>MAP</td>
<td>0.94</td>
<td>0.83</td>
</tr>
<tr>
<td>Creatinine</td>
<td>-0.48</td>
<td>-0.50</td>
</tr>
<tr>
<td>CVP</td>
<td>0.26</td>
<td>0.11</td>
</tr>
<tr>
<td>Urine outcome and fluid balance</td>
<td>0.60</td>
<td>0.25</td>
</tr>
<tr>
<td>PCT</td>
<td>-0.54</td>
<td>-0.43</td>
</tr>
<tr>
<td>WBC</td>
<td>-0.024</td>
<td>-0.27</td>
</tr>
<tr>
<td>CRP</td>
<td>-0.28</td>
<td>-0.31</td>
</tr>
<tr>
<td>Diametri I CT</td>
<td>0.26</td>
<td></td>
</tr>
</tbody>
</table>

Figure 1. Determination of IAP correlations and hospital mortalities according to APACHE II, IMP, SOFA and MODS mortality indices.
References