

## The Role of Biomarkers and Intra-Abdominal Pressure in Diagnosing and Predicting Mortality of Intra-Abdominal Infections

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### Abstract

Early diagnosis of intra-abdominal infections is imperative in surgery departments, and there have been constant efforts to find appropriate biomarkers that can aid early diagnosis of infection. Here, we aimed to determine the role of procalcitonin (PCT), C-reactive protein (CRP), triglycerides (TG), partial prothrombin time (PPT), leucocytes (LE) and intra-abdominal pressure (IAP) in the diagnosis and prognosis of intra-abdominal infections.

This was a prospective controlled study of 80 hospitalized patients who had undergone surgery as a result of acute abdomen.

Analyses based on infection severity showed increased PCT, TG, PTT and IAP in the septic shock, severe sepsis and systemic inflammatory response syndrome (SIRS)/sepsis groups; there was a significant statistical difference based on infection category. Based on infection severity, the mean CRP and LE count values were not significantly different. In the sepsis group, sensitivity was highest for CRP (76.79%), LE count (82.14%) and IAP (88%). In the septic shock group, PCT levels within the 17.56 ng/mL threshold had 87.5% sensitivity and 88.9% specificity. IAP sensitivity was high in the sepsis and septic shock groups (88% and 70.5%, respectively) but its specificity was low.

Serial biomarker measurements show the advantage of using PCT, PTT and TG for determining the severity of the condition, whereas CRP and LE count are indicators of the source of infection. Moreover, together with scoring systems for predicting mortality (APACHE II, SOFA, MODS, IMP), PCT, PTT and TG are important guides of the course of illness.

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### Introduction

Abdominal pathologies that progress to abdominal sepsis are relatively common in routine surgery service, and have a mortality rate of 30–50%.<sup>1,2</sup> Due to the body's complex response to sepsis, preoperative diagnosis and treatment criteria are insufficiently reliable, or have not been developed.<sup>2,3</sup>

Given the evident diagnostic and treatment challenges of intra-abdominal infections, efforts have been made to find

biomarkers that can aid early diagnosis of infection. Early detection and adequate treatment are essential for minimising complications in patients with acute abdomen.<sup>4,5,6,7</sup> Scoring systems such as APACHE II (Acute Physiology and Chronic Health Evaluation II), SOFA (Sequential Organ Failure Assessment), SAPS II (simplified acute physiology score II), MODS (multiple organ dysfunction score) and Mannheim peritonitis index (MPI) are valuable prognostic tools.<sup>8,9</sup> Procalcitonin (PCT) is an important assessment tool for early detection of disease progression to sepsis.<sup>10,11</sup> PCT was discovered in 1975 by a group of Spanish researchers led by Moya and Nieto.<sup>6</sup> It is a precursor to calcitonin, which is produced in the C cells of the thyroid gland.<sup>12</sup> PCT > 0.4 ng/mL is considered abnormal and indicates sepsis.<sup>13</sup> C-reactive protein (CRP) is the first acute-phase protein to be described. It is named after its capacity to precipitate the non-

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proteinic somatic fraction (fraction C) of *Streptococcus pneumoniae*. Surgical trauma increases CRP levels, which reduces its diagnostic value in early post-surgical infection.<sup>14</sup>  
<sup>15</sup> It is thought that lipid metabolism disorders are due to tumour necrosis factor alpha (TNF- $\alpha$ ) release, which increases serum triglyceride (TG) levels via increased hepatic production.<sup>16, 17</sup> and reduced lipoprotein lipase activity in fat tissue.<sup>18</sup>  
<sup>19</sup> In recent years, there has been interest in intra-abdominal hypertension (IAH), defined as the pathological increase of intra-abdominal pressure (IAP) > 12 mmHg.<sup>20</sup> Some abdominal clinical conditions (peritonitis, ileus, volvulus, pancreatitis, complications after abdominal surgery) and systemic conditions (sepsis, mechanical ventilation, pneumonia, burns) are related to IAH.<sup>20</sup> Abnormal coagulation tests obtained in sepsis can have serious effects on blood clotting in the human body. If the partial prothrombin time (PTT) is too high, mortality is increased in patients admitted to hospital with suspected infection.<sup>21</sup>

## Materials and methods

This was a non-randomized study of 80 patients performed at the University Clinic Centre of Kosovo in Prishtina between August 2018 and January 2019. We aimed to evaluate the efficacy of biomarkers (PCT, CRP, TG, PTT, leucocytes [LE]) and IAP for the diagnosis and prognosis of intra-abdominal infections. The study protocol was approved by the Ethics Committee of the Faculty of Medicine at the University of Pristina, and consent was obtained from all participants or their relatives.

**Inclusion Criteria:** All patients aged >18 years diagnosed with acute abdomen and systemic inflammatory response syndrome (SIRS) who had also undergone surgical intervention.

**Exclusion Criteria:** Patients with autoimmune disease, acute hepatic failure, diabetes, immunosuppression, who were pregnant, treated with glucocorticoids and for hypertriglyceridemia, and those who declined to be included in the study.

## Protocol and Treatment

The basic study criteria was the measurement of PCT, CRP, TG, PTT, LE count and IAP. Clinical examination and laboratory and imaging investigations were performed at the

University Clinical Centre of Kosovo. All biomarker levels were measured preoperatively, on postoperative day 1, 4 and 7, and subsequently if clinically indicated. The baseline criterion was the preoperative measurement of IAP every 4 h, and it was evaluated as IAH if the average of these measurements was >12 mmHg. In addition, the measurement was performed postoperatively three times in 24 h, and the mean calculated for each day. The measurement was continued until IAP normalization. The IAP was measured by the method evaluated by Kron. We performed laboratory measurements and analyses relevant to the designation of IAH/ACS (abdominal compartment syndrome), MODS, APACHE II, SOFA, MPI and MAP (mean arterial pressure). Based on the clinical, laboratory and general findings, we classified intra-abdominal infection severity into SIRS/sepsis, severe sepsis and septic shock groups. At the same time, patients were grouped based on the IAP values as Grade I (IAP 12–15 mmHg), Grade II (IAP 16–20 mmHg) and Grade III (IAP 21–25 mmHg). The biomarker values were compared with that from the above scoring systems to evaluate the prognostic role of the biomarkers.

## Statistical Analysis

The results were stratified based on intra-abdominal infection severity. Age, sex and the relevant scoring systems were also used. Statistical data were processed using SPSS 22.0. The arithmetic mean, standard deviation (SD) and minimal and maximal values were calculated. Spearman's correlation coefficient was used for non-parametric data. Qualitative data were tested with the  $\chi^2$  test and Fisher's exact test; quantitative data with normal dispersion were tested with the *t*-test and one-way analysis of variance (ANOVA), whereas quantitative data with abnormal dispersion were tested with the Mann-Whitney and Kruskal-Wallis tests. *P* < 0.05 indicated a significant difference.

## Results

In the total cohort of 80 patients, 50 (62%) were male and 30 (38%) were female. The average age was 41.4 years (SD 19.6). Patients were assigned to the SIRS/sepsis, severe sepsis or septic shock group.

The preoperative mean PCT was 13.1 ng/mL (SD 28.5 ng/mL); PCT was increased in

the three groups, but the Kruskal-Wallis test (KW) revealed a significant statistical difference between the mean PCT on the preoperative day (KW = 13.3) and postoperative days 1 (KW = 12.1), 4 (KW = 20.4) and 7 (KW = 30.2) based on infection category. In the septic shock group, the mean PCT remained high postoperatively. In the severe sepsis and sepsis groups, the mean PCT decreased postoperatively. There were significant statistical differences on other postoperative days as well.

The mean preoperative CRP value was 129.7 mg/L (SD 101.3 mg/L); the Kruskal-Wallis test did not reveal a significant statistical difference between the mean CRP preoperatively (KW = 1.68) and on postoperative days 1 (KW = 0.0224) and 4 (KW = 2.66) based on infection category. The mean CRP values were significantly statistically different only on postoperative day 7 (KW = 10.6). The mean preoperative TG value was 1.72 mol/L (SD 1.06 mg/L); TG was increased in the septic shock group and slightly increased in the severe sepsis group, whereas the SIRS/sepsis group had borderline normal values. In the septic shock group, the mean TG value remained high postoperatively. In the severe sepsis group, it decreased postoperatively, and was within normal range in the SIRS/sepsis group. The preoperative mean LE count was 14.6 mm<sup>3</sup> (SD 6.4 mm<sup>3</sup>) and was not significantly different based on infection severity (one-way ANOVA, F = 2.12, P = 0.132). The mean LE counts were statistically significantly different in all three groups postoperatively (day 1, F = 3.77; day 4, KW = 9.53; day 7, KW = 6.88).

The mean PTT values were statistically significantly different based on infection severity preoperatively (KW = 8.06) and postoperatively (day 1, KW = 10.1; day 4, KW = 12.3; day 7, KW = 15.7).

Analysis based on infection severity revealed increased IAP in all groups; the difference was statistically significant by infection category pre-surgery and in the four postoperative days. IAH was present in 87.5% of cases. The preoperative mean IAP was 15.6 mmHg (SD 2.9 mmHg); IAP was increased in the septic shock (18.4 mmHg [SD 2.8 mmHg]) and severe sepsis groups (18.3 mmHg [SD 3.2 mmHg]). The SIRS/sepsis group had slightly increased IAP: 14.7 mmHg (SD 2.3 mmHg). The Kruskal-Wallis test showed a significant

difference between the groups (KW = 17.53, P = 0.0002). In the following days, the IAP began to decrease due to surgical decompression; however, the significant difference between groups persisted (Table 1).

Abdominal emergencies (n = 80)				
	SIRS/sepsis Mean ± SD	Severe sepsis Mean ± SD	Septic shock Mean SD	± P
Preoperative				
PCT	3.1 ± 5.6	22.5 ± 36.7	67.8 50.9	± 0.0015 <sup>a</sup>
CRP	133.1 ± 90.5	194.2 ± 72.3	177.9 123.7	± 0.431 <sup>a</sup>
TG	1.34 ± 0.90	2.50 ± 0.75	3.27 0.34	± <0.0001 <sup>a</sup>
LE count	14.2 ± 4.1	18.4 ± 11.7	11.5 8.2	± 0.132 <sup>b</sup>
PTT	38.2 ± 7.4	34.8 ± 9.7	29.9 2.8	± 0.017 <sup>a</sup>
IAP	15.1 ± 2.2	18.1 ± 3.1	18.5 2.6	± 0.0002 <sup>a</sup>
Postoperative day 1				
PCT	2.1 ± 2.6	6.5 ± 7.6	62.4 48.2	± 0.0024 <sup>a</sup>
CRP	118.8 ± 74.7	121.7 ± 90.6	228.8 221.2	± 0.894 <sup>a</sup>
TG	1.30 ± 0.8	2.27 ± 0.70	3.13 0.48	± <0.0001 <sup>a</sup>
LE count	12.4 ± 4.1	17.6 ± 7.0	13.9 6.8	± 0.03 <sup>b</sup>
PTT	41.4 ± 10.9	33.5 ± 5.6	29.9 1.7	± 0.009 <sup>a</sup>
IAP	16.1 ± 5.1	16.5 ± 3.4	11.9 1.9	± 0.0002 <sup>a</sup>
Postoperative day 4				
PCT	0.8 ± 0.8	3.3 ± 3.4	43.3 37.3	± <0.0001 <sup>a</sup>
CRP	87.8 ± 67.8	102.4 ± 58.2	134.2 104.2	± 0.264 <sup>a</sup>
TG	1.23 ± 0.74	2.00 ± 0.47	3.10 0.46	± <0.0001 <sup>a</sup>
LE count	10.8 ± 3.2	17.5 ± 7.3	19.1 9.3	± 0.0008 <sup>a</sup>
PTT	42.2 ± 6.9	31.8 ± 4.3	29.4 2.0	± 0.007 <sup>a</sup>
IAP	16.6 ± 3.9	14.5 ± 3.7	10.2 2.5	± <0.0001 <sup>a</sup>
Postoperative day 7				
PCT	0.3 ± 0.4	1.3 ± 1.7	25.7 15.9	± <0.0001 <sup>a</sup>
CRP	44.6 ± 27.2	111.9 ± 111.4	133.1 100.4	± 0.0049 <sup>a</sup>
TG	1.22 ± 0.73	2.02 ± 0.51	3.42 0.47	± <0.0001 <sup>a</sup>
LE	8.6 ± 1.9	13.8 ± 6.6	17.6 9.6	± 0.07 <sup>a</sup>
PTT	47.5 ± 13.2	32.9 ± 3.7	29.2 1.7	± 0.005 <sup>a</sup>
IAP	16.12 ± 0.99	12.2 ± 3.66	9.7 ± 2.1	0.0031 <sup>a</sup>

<sup>a</sup> Kruskal-Wallis, <sup>b</sup> one-way ANOVA

**Table 1.** Comparison of PCT, CRP, PTT, TG and LE count in urgent abdominal presentation based on infection category.

The optimum cut-off value for PCT in abdominal sepsis was 0.5 ng/mL, and had 78.57% sensitivity and 37.5.0% specificity. At the threshold value of 2.1 ng/mL, PCT sensitivity was decreased. The cut-off value with the best diagnostic accuracy for CRP in sepsis was 70 mg/L, which had 76.79% sensitivity and 33.33% specificity. At the threshold value of 110 mg/L, CRP sensitivity decreased (Table 2).

Sepsis					
	Sensitivity (%)	Specificity (%)	Accuracy (%)	PPV (%)	NPV (%)
PCT (0.5 ng/mL)	78.57	37.5	66.3	74.5	42.8
PCT (2.1 ng/mL)	51.7	50.0	51.3	78.3	22.8
CRP (70 mg/L)	76.79	33.33	63.75	72.88	38.0
CRP (110 mg/L)	50.9	44.4	49.3	73.6	44.4
TG (186 mmol/L)	41.07	54.17	45.0	67.64	28.2
PTT (30 sec)	75.0	12.50	56.25	66.6	17.64
LE (10 × 10 <sup>9</sup> /L)	82.14	33.33	67.50	74.1	44.4
IAP (12.5 mmHg)	88.0	26.67	65.00	66.6	57.1

PPV – Positive Predictive Value  
 NPV – Negative Predictive Value

**Table 2.** Sensitivity and specificity of biomarkers and IAP in abdominal sepsis.

The optimum cut-off value for PCT in abdominal septic shock was 17.56 ng/mL, which had high sensitivity and specificity. In septic shock, LE count did not have high sensitivity and specificity at the threshold value of 15 × 10<sup>9</sup> cells/L. At the threshold value of 136 mg/L, CRP had 71% sensitivity and 53% specificity. At the threshold of 2.20 mmol/L, TG had 75% sensitivity, 57.1% specificity, positive predictive value (PPV) of 50% and negative predictive value (NPV) of 22.2%. The cut-off value with the best diagnostic accuracy for IAP in septic shock was 14.7 mmHg, which had high sensitivity but low specificity. PTT had the highest sensitivity among all parameters (Table 3).

The PCT, PTT and TG levels were well correlated with the SOFA, APACHE II, MPI and MODS scores. Meanwhile, LE count and CRP level correlated poorly with the scores. Overall, SOFA, APACHE II, MODS and MPI scores were highest among the patients with septic shock (Table 4).

Septic shock					
	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
PCT (17.56 ng/mL)	87.5	88.9	53.8	83.3	66.6
CRP (136 mg/L)	71.0	53.0	17.8	92.8	12.5
TG (2.20 mmol/L)	75.0	57.1	50.0	88.8	22.2
PTT (32 sec)	100	23.6	12.6	100.0	31.2
LE (15 × 10 <sup>9</sup> /L)	62.5	52.7	12.8	92.6	53.7
IAP (14.7 mmHg)	75	42.8	18.1	88.2	16.0

**Table 3.** Sensitivity and specificity of biomarkers and IAP in abdominal septic shock.

Abdominal emergencies (n = 80)				
	Septic shock (n = 8)	Severe sepsis (n = 16)	SIRS/sepsis (n = 56)	P
	Mean ± SD	Mean ± SD	Mean ± SD	0.184 <sup>a</sup>
MODS	12.8 ± 3.8	7.3 ± 3.6	2 ± 1.3	<0.0001 <sup>a</sup>
MPI	34.8 ± 4.3	26.1 ± 5.1	13.8 ± 8.1	<0.0001 <sup>a</sup>
APACHE II	34 ± 9.5	19.5 ± 6.3	9.9 ± 5.1	<0.0001 <sup>a</sup>
SOFA	17.8 ± 7.6	10.5 ± 3.8	5.2 ± 2.4	<0.0001 <sup>a</sup>

<sup>a</sup> Kruskal-Wallis test

**Table 4.** Predictive biomarkers and IAP parameters based on intra-abdominal infection severity and outcome.

The MODS and SOFA scores were superior compared to the other scores, with high sensitivity and specificity for predicting mortality in patients with sepsis. Using the two cut-offs showed that the APACHE II and MPI scores were sensitive but less specific for predicting mortality. The patients who died had high preoperative mean biomarker values: PCT, 34.6 ± 28.9 ng/mL; CRP, 204.63 ± 13.4 mg/L; TG, 2.67 ± 0.43 mmol/L; LE, 15.54 ± 41.8 × 10<sup>9</sup>/L; PTT, 35.5 ± 32.0 sec. PCT, LE, PTT and TG were more sensitive but insufficiently specific for predicting mortality. CRP was less sensitive and specific for predicting mortality (Table 5).



	Cut-off	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
APACHE II	≥13 points	90.0	54.0	25.0	96.6	59.6
APACHE II	≥15 points	90.0	67.9	32.0	97.2	70.9
SOFA	≥10 points	90.0	35.0	38.0	87.5	53.5
SOFA	≥11 points	80.0	84.2	70.0	88.8	82.1
MPI	≥20 points	90.0	45.2	23.6	96.0	52.3
MPI	≥25 points	90.0	54.7	27.2	96.6	62.2
MODS	≥3 points	90.0	91.4	69.2	97.7	91.2
MODS	≥5 points	90.0	68.0	37.5	96.9	71.9
PCT	3.6 ng/mL	70.0	46.0	20.5	88.4	50.0
LE	14.9 × 10 <sup>9</sup> /L	70.0	61.4	20.5	93.4	62.5
CRP	170 mg/L	40.0	42.4	17.3	70.0	41.8
TG	3.1 mmol/L	60.0	39.3	23.0	76.4	41.8
PTT	30 sec	90.0	40.7	36.0	91.6	54.0
IAP	16.1 mmHg	50.0	59.0	19.2	86.1	58.0

**Table 5.** Sensitivity and specificity in predicting mortality in patients with sepsis.

## Discussion

In this clinical study, we evaluated the predictive role of PCT, CRP, TG, LE, PTT and IAP in intra-abdominal infections. Our findings indicate a significant statistical difference between the mean PCT, PTT and TG values preoperatively and on postoperative days 1, 4, 7 according to infection category. The preoperative LE counts and CRP values were not significantly different based on infection severity. The mean LE count was statistically significantly different in all three groups postoperatively. PCT values increased before CRP values did, and also decreased faster than CRP values. CRP was also high in cases with less marked systemic inflammation and organ dysfunction; however, it did not increase in cases with disease progression, unlike PCT, PTT and TG, which increased significantly in patients with organ dysfunction, severe sepsis and septic shock. Our findings correspond to that of other authors. Gregoric et al. reported high PCT values in the sepsis group, which were significantly different compared to the SIRS group, and PCT value correlated with peritonitis severity.<sup>22</sup> Others have concluded that the PCT value increases remarkably before CRP, that PCT decreases

faster and is significantly increased, especially in cases with septic shock and severe sepsis.<sup>20, 23, 24</sup> Bell et al. concluded that PCT is more important than CRP for differentiating bacterial infections from infections from other causes.<sup>25</sup> Nargis et al. show a difference between CRP values based on infection category, highlighting the fact that the authors did not include SIRS cases.<sup>26</sup> Yet others have concluded that CRP does not differentiate levels of severity in sepsis.<sup>27, 28</sup> In the present study, we did not obtain a significant statistical difference between the preoperative CRP values based on infection category. Our study shows that PCT is superior for evaluating the disease severity.

Our findings show that TG was increased in patients with septic shock and slightly increased in severe sepsis, whereas the SIRS/sepsis group had normal TG values. TG remained higher in the cases with mortality. Our data correspond to that of other authors who defined hypertriglyceridemia as a risk factor of mortality in patients with sepsis.<sup>29, 30</sup>

The preoperative mean LE counts were higher in sepsis, severe sepsis and septic shock, but not significantly different between the groups; we believe this is a result of neutropenia in some cases with septic shock and severe sepsis.

PTT was increased noticeably in patients with septic shock and severe sepsis, and remained high in the patients that died. These results correspond with that of other authors who concluded that changes in coagulation factors and the impact of PTT play a role in disease prognosis.<sup>31, 32</sup> The change in PTT values and other coagulation factors is linked to organ dysfunction and with 28-day mortality.<sup>32</sup>

Our findings indicate a significant statistical difference between the mean IAP values preoperatively and on postoperative days 1, 4, 7 based on infection category, even though the grade of IAP does not predict the disease severity. Our data do not correspond with that of Regueira et al., who reported that, in 80% of cases, septic shock and severe sepsis were accompanied by grade II and grade III IAH, respectively.<sup>33</sup> According to De Waele et al., IAH is very prevalent in cases with sepsis, severe sepsis and septic shock.<sup>34</sup>

In the present study, we analysed the sensitivity, specificity, PPV and NPV of biomarkers and IAP in sepsis. The values were determined using an optimal cut-off. PCT, CRP,

PTT, LE count and IAP had increased sensitivity but not specificity. TG had lower sensitivity and specificity.

Our data correspond with that of many authors. After analysing the data of each parameter, we conclude that our findings are both similar and dissimilar with that of other authors. Compared to the study of Kalem et al., our results do not match the results for CRP and LE; In their study, CRP had high sensitivity and LE count had high specificity, while PCT had similar sensitivity and specificity to that of our study.<sup>35</sup> Sorsa reported that the LE count had 59.5% sensitivity, 79.6% specificity, PPV of 52% and NPV of 64.5%, while CRP had 65.6% sensitivity, 78% specificity, PPV of 42% and NPV of 91%.<sup>36</sup> which do not correspond with our data.

We found increased sensitivity, specificity, PPV and NPV of PCT in septic shock, while TG and PTT had increased sensitivity. Sharma et al. reported that at a cut-off of 9.9 ng/mL, PCT had 91.7% sensitivity and 74.2% specificity.<sup>37</sup> We found that the most accurate diagnostic cut-off PCT value for septic shock was 17.5 ng/mL. Nargis and colleagues<sup>26</sup> on the other hand, highlighted that the diagnostic accuracy of PCT had 75% specificity and 76% sensitivity, with PPV and NPV of 89% and 50%, respectively.

The mean PCT value in septic shock was 34.6 ng/mL; the mean MODS score was 12.8 points (SD 3.9 points). These data correspond with other literature, where PCT correlated with MODS score whereby its value was low in cases with weak inflammatory response or single organ dysfunction.<sup>24</sup>

In our study, the correlation of PCT and the MPI was of intermediate significance (KW = 0.623,  $P < 0.0001$ ), which does not correspond with the findings of Wacha and Linder<sup>38</sup> who concluded that MPI score does not correlate with PCT.

PCT values, but not CRP values, have been significantly correlated with APACHE II score.<sup>39,40</sup> Our data correspond with this.

Our findings show that high PCT and TG levels correspond with high SOFA score, but that CRP does not correlate with SOFA score. Meisner et al. measured PCT, CRP, SOFA and APACHE II daily for 5 days in 40 patients with SIRS/sepsis, and found that high SOFA score correlated with high PCT values.<sup>24</sup> CRP, on the other hand, was increased even in cases with low SOFA score, meaning it does not yield data

on the progression of inflammation or the level of organ dysfunction.<sup>39,40</sup> TG values do not correlate well with SOFA score; nonetheless, combining SOFA score with TG values is a better predictor of mortality compared to SOFA score alone.<sup>45,46</sup>

Our results show that the LE counts do not correlate with the above scoring systems for predicting mortality. These data do not correspond with the data of other authors. Dimitrios et al. concluded on the significant correlation of LE count with SOFA and APACHE scores.<sup>41</sup>

We measured biomarker sensitivity, specificity, PPV and NPV; and IAP; and the APACHE II, SOFA, MODS and MPI scores for predicting mortality. All scoring systems had high sensitivity for predicting mortality, while the MODS and SOFA scores had increased specificity. The APACHE II score had high sensitivity for both cut-offs but had higher specificity at the cut-off of >15 points. These results do not fully match that of Kulkarni et al.<sup>42</sup>

Our results show that the SOFA score has high sensitivity but low specificity for the cut-off of 10 points; specificity increased for the cut-off of 11 points. These results do not correspond with the data of Wang et al., who concluded that the most accurate index is the SOFA score (area under the curve [AUC] = 0.889,  $P = 0.000$ ; when the threshold value was 9.50, sensitivity was 81.2% and specificity was 83.5%).<sup>43</sup>

PTT, PCT and LE count had high sensitivity for predicting mortality, while LE count had high specificity. CRP did not have high sensitivity and specificity for disease prognosis, which corresponds to the data of Kopterides et al.<sup>44</sup> Our PCT results do not fully match that of Wang et al., who concluded that, at the PCT threshold value of 3.94 ng/mL, sensitivity was 84.7% and specificity was 94.1%.<sup>43</sup>

## Conclusions

There are advantages and benefits to using PCT, PPT and TG for evaluating infection severity, whereas PCT, TG and IAP provide data on the course of illness. CRP and LE count, on the other hand, indicate the presence of infection, but their values do not show a significant difference in terms of classification of infection severity.

## Declaration of Interest

The authors report no conflict of interest.

## References

1. Calandra T, Cohen J. The International Sepsis Forum Consensus Conference on Definitions of Infection in the Intensive Care Unit. *Crit Care Med.* 2005 Jul;33(7):1538–48.
2. Crandall M, West MA. Evaluation of the abdomen in the critically ill patient: opening the black box. *Curr Opin Intern Med.* 2006 Oct;5(5):466–72.
3. Gullo A, Bianco N, Berlot G. Management of severe sepsis and septic shock: challenges and recommendations. *Crit Care Clin.* 2006 Jul;22(3):489–501, ix.
4. Emmi V, Sganga G. [Diagnosis of intra-abdominal infections: clinical findings and imaging]. *Infez Med.* 2008 Feb;16 Suppl 1:19–30.
5. Bone RC, Balk RA, Cerra FB, Dellinger RP, Fein AM, Knaus WA, et al. Definitions for Sepsis and Organ Failure and Guidelines for the Use of Innovative Therapies in Sepsis. *Chest.* 1992 Jun;101(6):1644–55.
6. Moya F, Nieto ACJ. Calcitonin Biosynthesis: Evidence for a Precursor. *Eur J Biochem.* 1975 Jul;55(2):407–13.
7. Foinant M, Lipiecka E, Buc E et al. Impact of computed tomography on patient's care in nontraumatic acute abdomen: 90 patients. *J Radiol.* 2007;88(4):559–66.
8. Giamarellos-Bourboulis EJ, Norrby-Teglund A, Mylona V, Savva A, Tsangaris I, Dimopoulou I, et al. Risk assessment in sepsis: a new prognostication rule by APACHE II score and serum soluble urokinase plasminogen activator receptor. *Crit Care.* 2012;16(4):R149.
9. Horiuchi A, Watanabe Y, Doi T, Sato K, Yukumi S, Yoshida M, et al. Evaluation of prognostic factors and scoring system in colonic perforation. *World J Gastroenterol.* 2007 Jun;13(23):3228–31.
10. Schmitz RPH, Brunkhorst FM. Sepsis biomarkers and pathogen detection methods: State of the art. *Sanamed.* 9(1):49–61.
11. Novotny AR, Emmanuel K, Hueser N, Knebel C, Kriner M, Ulm K, Bartels H, Siebert JRH. Procalcitonin ratio indicates successful surgical treatment of abdominal sepsis. *Surgery.* 2009 Jan;145(1):20–6.
12. Wiedermann FJ, Kaneider N, Egger P, Tiefenthaler WWC. Migration of human monocytes in response to procalcitonin. *Crit Care Med.* 2002;30:1112–7.
13. Meisner M. Update on Procalcitonin Measurements. *Ann Lab Med.* 2014 Jul;34(4):263.
14. Lindberg M, Åsberg A, Myrvold HE, Hole A, Rydning A, Bjerve KS. Reference intervals for procalcitonin and C-reactive protein after major abdominal surgery. *Scand J Clin Lab Invest.* 2002 Jan;62(3):189–94.
15. Oberhofer D, Rumenjak V, Lazić J, Vucić N. [Inflammatory indicators in patients after surgery of the large intestine]. *Acta Med Croatica.* 2006 Dec;60(5):429–33.
16. Feingold KR, Staprans I, Memon RA, Moser AH, Shigenaga JK, Doerrler W, et al. Endotoxin rapidly induces changes in lipid metabolism that produce hypertriglyceridemia: low doses stimulate hepatic triglyceride production while high doses inhibit clearance. *J Lipid Res.* 1992 Dec;33(12):1765–76.
17. Feingold KR, Grunfeld C. Tumor necrosis factor- $\alpha$  stimulates hepatic lipogenesis in the rat in vivo. *J Clin Invest.* 1987 Jul;80(1):184–90.
18. Grunfeld C, Gulli R, Moser AH, Gavin LA, Feingold KR. Effect of tumor necrosis factor administration in vivo on lipoprotein lipase activity in various tissues of the rat. *J Lipid Res.* 1989 Apr;30(4):579–85.
19. Semb H, Peterson J, ... JT-J of B, 1987 U. Multiple effects of tumor necrosis factor on lipoprotein lipase in vivo. *J Biol Chem.* 1987;262(17):8390–4.
20. Castelli GP, Pognoni CCM. Procalcitonin, C-reactive protein, white blood cells and SOFA score in ICU: diagnosis and monitoring of sepsis. *Minerva Anesthesiol.* 2006;72(1–2):99–80.
21. Fischer CM, Yano K, Aird WC, Shapiro NI. Abnormal Coagulation Tests Obtained in the Emergency Department are Associated with Mortality in Patients with Suspected Infection. *J Emerg Med.* 2012 Feb;42(2):127–32.
22. Gregoric P, Pavle G, Sijacki A, Ana S, Stankovic S, Sanja S, et al. SIRS score on admission and initial concentration of IL-6 as severe acute pancreatitis outcome predictors. *Hepatogastroenterology.* 2010;57(98):349–53.
23. Harbarth S. Diagnostic Value of Procalcitonin, Interleukin-6, and Interleukin-8 in Critically Ill Patients Admitted with Suspected Sepsis. *Am J Respir Crit Care Med.* 2001 Aug;164(3):396–402.
24. Meisner M, Tschaikowsky K, Palmaers T, Schmidt J. Comparison of procalcitonin (PCT) and C-reactive protein (CRP) plasma concentrations at different SOFA scores during the course of sepsis and MODS. *Crit Care.* 1999 Mar;3(1):45.
25. Bell K, Wattie M, Byth K, Silvestrini R, Clark P, Stachowski E, et al. Procalcitonin: A Marker of Bacteraemia in SIRS. *Anaesth Intensive Care.* 2003 Dec;31(6):629–36.
26. Nargis W, Ibrahim M, Ahamed BU. Procalcitonin versus C-reactive protein: Usefulness as biomarker of sepsis in ICU patient. *Int J Crit Illn Inj Sci.* 2014 Jul;4(3):195–9.
27. Castelli G, Pognani C, Meisner M, Stuardi A, Bellomi D, Sgarbi L. Procalcitonin and C-reactive protein during systemic inflammatory response syndrome, sepsis and organ dysfunction. *Crit Care.* 2004 Jun;8(4):R234.
28. Maraghi SEL, Yehia A, Mahmoud O, Abd Hamid AEL, El Maraghi S. Procalcitonin Versus C-Reactive Protein at Different SOFA Scores in I.C.U. Sepsis: Diagnostic Value and Therapeutic Implications. *Med J Cairo Univ.* 2014;82(1):29–36.
29. Cetinkaya A, Erden A, Avci D, Karagoz H, Karahan S, Basak M, et al. Is hypertriglyceridemia a prognostic factor in sepsis? *Ther Clin Risk Manag.* 2014;10:147–50.
30. Harris HW, Grunfeld C, Feingold KR, Rapp JH. Human very low density lipoproteins and chylomicrons can protect against endotoxin-induced death in mice. *J Clin Invest.* 1990 Sep;86(3):696–702.
31. Angstwurm MWA, Dempfle C-E, Spannagl M. New disseminated intravascular coagulation score: A useful tool to predict mortality in comparison with Acute Physiology and Chronic Health Evaluation II and Logistic Organ Dysfunction scores. *Crit Care Med.* 2006 Feb;34(2):314–20.
32. Dhainaut J-F, Shorr AF, Macias WL, Kollef MJ, Levi M, Reinhart K, et al. Dynamic evolution of coagulopathy in the first day of severe sepsis: Relationship with mortality and organ failure\*. *Crit Care Med.* 2005 Feb;33(2):341–8.
33. Regueira T, Bruhn A, Hasbun P, Aguirre M, Romero C, Llanos O, et al. Intra-abdominal hypertension: Incidence and association with organ dysfunction during early septic shock. *J Crit Care.* 2008 Dec;23(4):461–7.
34. De Waele JJ, De laet I. Intra-Abdominal Hypertension and MODS. In: *Sepsis Management.* Berlin, Heidelberg: Springer Berlin Heidelberg; 2012. p. 59–71.
35. Kalem F, Durmaz S, Ozdemir B, Gul Ergun A, Ertugrul O. The diagnostic value of procalcitonin, WBC, and CRP in diagnosis of lower respiratory tract infections in elderly patients. *Biomed Res.* 2017;28(13):1012–5.
36. Sorsa A. Diagnostic Significance of White Blood Cell Count and C-Reactive Protein in Neonatal Sepsis; Asella Referral Hospital, South East Ethiopia. *Open Microbiol J.* 2018;12:209–17.
37. Sharma R, Vijayakumar M. Procalcitonin for improved assessment and an answer to sepsis dilemma in critically ill - a myth, a hype, or a reality? *Nitte Univ J Heal Sci.* 2014;4(1):57–65.
38. Wacha H, Linder MMFU. Mannheim peritonitis index - prediction of risk of death from peritonitis: construction of a statistical and validation of an empirically based index. *Theor Surg.* 1987;1:169–77.

39. López F. Procalcitonin (PCT), C reactive protein (CRP) and its correlation with severity in early sepsis. *Clin Rev Opin.* 2011;3(3):26–31.
40. Wang S, Chen D. [The correlation between procalcitonin, C-reactive protein and severity scores in patients with sepsis and their value in assessment of prognosis]. *Zhonghua Wei Zhong Bing Ji Jiu Yi Xue.* 2015 Feb;27(2):97–101.
41. Dimitrios V. Correlation between neutrophil-to-lymphocyte ratio and severity scores in septic patients upon hospital admission. A series of 50 patients. *sciendo.* 2018;56(3):153–7.
42. Kulkarni SV, Naik AS, Subramanian N. APACHE-II scoring system in perforative peritonitis. *Am J Surg.* 2007 Oct;194(4):549–52.
43. Wang Y, Wang D, Fu J, Liu Y. [Predictive value of SOFA, qSOFA score and traditional evaluation index on sepsis prognosis]. *Zhonghua Wei Zhong Bing Ji Jiu Yi Xue.* 2017 Aug;29(8):700–4.
44. Kopterides P, Siempos II, Tsangaris I, Tsantes A, Armaganidis A. Procalcitonin-guided algorithms of antibiotic therapy in the intensive care unit: A systematic review and meta-analysis of randomized controlled trials. *Crit Care Med.* 2010 Nov;38(11):2229–41.
45. Lee SH, Park MS, Park BH, Jung WJ, Lee IS, Kim SY, et al. Prognostic Implications of Serum Lipid Metabolism over Time during Sepsis. *Biomed Res Int.* 2015 Aug;2015:1–8.
46. Li Z, Wang H, Liu J, Chen B, Li G. Serum soluble triggering receptor expressed on myeloid cells-1 and procalcitonin can reflect sepsis severity and predict prognosis: a prospective cohort study. *Mediators Inflamm.* 2014 Feb;2014:641039.