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Systemic Inflammatory Response Syndrome in Surgical Patients

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ABSTRACT

Objective: To determine the incidence of systemic inflammatory response of the organism in surgical patients and its impact on the outcome of treatment. **Methods:** A prospective study was conducted on 60 patients undergoing abdominal surgical procedures, between January 2014 and December 2015 in the Surgery Clinic at the University Clinical Center Tuzla. Two groups of thirty were formed by the method of consecutive sampling. The first group consisted of subjects who were prepared for elective abdominal surgery (laparoscopic cholecystectomy), and the second group subjects underwent an emergency surgery due to acute abdomen (laparoscopic cholecystectomy). **Results:** The body temperature difference was statistically significant between the two investigated groups in all stages ($c^2: t_0=3,486; t_1=3,098; t_2=2,453, t: t_0=-11,210; t_1=-7,360; t_2=-4,927, p < 0,05$). Non-elective surgery group had a statistical significant difference of the heart rate at all stages ($c^2: t_0=3,873; t_1=3,357; t_2=3,227, t: t_0=-16,524; t_1=-10,407; t_2=-9,842, p < 0,05$). There is a statistically significant difference in the pCO₂ values in all stages between groups ($c^2: t_0=2,582; t_1=1,678; t_2=1,162, t: t_0=4,323; t_1=2,653; t_2=2,229, p < 0,05$). The SIRS score has a good positive correlation with the length of treatment, while the correlation with the outcome of treatment has no statistical significance. **Conclusion:** Inflammation scores monitoring in surgical patients is important for the surgical treatment success analysis. By modifying the therapy and influencing the inflammatory response, the results of treatment are improved.

Keywords: systemic inflammatory response syndrome, inflammation, acute phase reaction.

1. INTRODUCTION

Stress is a set of noxious agents that adversely affect the body: trauma, shock, surgery, pain. The body's response to stress depends on the strength of the stressor and the body condition before the action of the stress agent. With better body condition the response to a stressful state is more turbulent (1). The stress response of a body implies hormonal and metabolic changes after injury or trauma. The systemic response to the surgical trauma implies the activation of the sympathetic nervous system, the endocrine response to stress, immunological and hematological changes (2). Inflammation is an expected, usually localized response of the body, followed by systemic signs of varying intensity, induced by tissue damage or destruction. Main goal of inflammation is to destroy, alleviate or eliminate provoking factors or to limit the size of the tissue damage, and to start the tissue repair (3, 4). If the inflammatory reaction of the body is not localized, it is affecting the whole body, within the systemic inflammatory

response of the organism. Systemic inflammatory response of the organism is the reflection of action of the acute phase reaction mediators. SIRS is a non-specific reaction caused by an acute insult in the body, which leads to the defense reaction of the body, with the goal to localize and eliminate endogenous or exogenous insult. Inflammatory cascade is a complex process that includes humoral and cellular responses, complement, and cytokines (5, 6). Objective of the study was to determine the incidence of systemic inflammatory response of the organism in surgical patients and its impact to the outcome of treatment.

2. MATERIALS AND METHODS

A prospective study was conducted on 60 patients undergoing abdominal surgical procedures, between January 2014 and December 2015 in the Surgery Clinic at the University Clinical Center Tuzla. Two groups of thirty were formed by the method of consecutive sampling. The first group (elective) consisted of subjects who were prepared for abdominal

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elective surgery (laparoscopic cholecystectomy), and the second group (non-elective) subjects underwent an emergency surgery due to acute abdomen (laparoscopic cholecystectomy). The subjects of both groups belonged both sexes, age from 18-70, and were the I-IV group of anesthesiology risk according to the classification of the American Association of Anesthesiologists (ASA). Patients were operated under general anesthesia. They all signed informed consent. Preoperatively we recorded data regarding name, gender, age, co-morbidity and parameters including body temperature, heart rate, pCO₂, number of leukocytes, which represent the initial value of the test parameters (t₀). The same parameters were analyzed 24 and 72 hours after the surgical procedure, which represents the value of t₁ and t₂. We valued the intensity of the inflammatory response of the body based on these SIRS score parameters: a) Body temperature higher than 38°C or lower than 36°C; b) Heart rate greater than 90 beats per minute; c) Respiratory frequency greater than 20 breaths per minute or pCO₂ less than 4.3 kPa; d) The number of leukocytes greater than 12,000 or less than 4,000, or the presence of more than 10% of immature neutrophils. Each positive parameter was given with one point. Two or more points indicate the systemic inflammatory response of the body. Statistical tests were done using the SPSS 19.0 software package. Variables were tested for normality with a Kolmogorov-Smirnov test. Standard methods of descriptive statistics were used: mean and standard deviation, t-test and χ^2 test for calculating the significant difference between the expected frequencies and the observed frequencies. The relationships between variables were tested using both Pearson and Spearman's correlation.

3. RESULTS

The study included two groups of 30 subjects aged 18 to 70 years. In the elective surgery group (Group 1), the average age was 47.53 ± 15.44, while the average age in the non-elective surgery group (Group 2) was 56.03 ± 20.10 years. In Group 1, the majority of subjects were 51-65 years of age, and in Group 2 they were 66-80 years old. Of the 60 analyzed patients, 26 were male and 34 were female. The majority of subjects were without co-morbidities. In the elective surgery group subjects were hospitalized for 3.40 ± 1 days hospitalization, while in the non-elective surgery group subjects were hospitalized for 8.70 ± 5.88 days (p < 0.05). All patients from the elective surgery group were discharged home, while 25 non-elective surgery group subjects were discharged while elderly 5 subjects died (p=0.023). The body temperature difference was statistically significant between the two investigated groups in all stages (c²: t₀=3,486; t₁=3,098; t₂=2,453, t: t₀=-11,210; t₁=-7,360; t₂=-4,927, p < 0,05). Wilcoxon's paired t-test showed that there was a statistically significant difference in body temperature at all stages in non-elective surgery group subjects, while in the elective surgery group, this difference only exists between Stage t₀ and t₁. Non-elective surgery group subjects had a statistical significant difference of the heart rate at all stages (c²: t₀=3,873; t₁=3,357; t₂=3,227, t: t₀=-

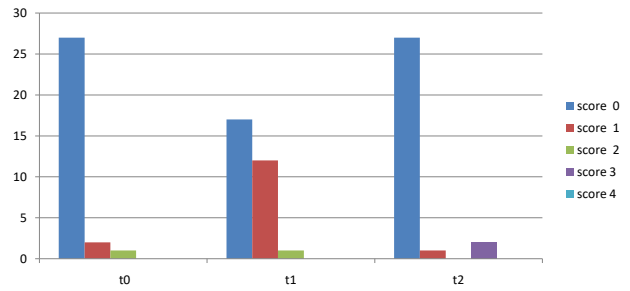


Figure 1. SIRS score of the elective surgery group subjects

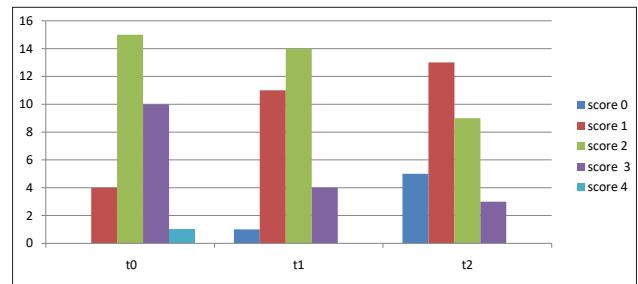


Figure 2. SIRS score of the non-elective surgery group subjects

Variable	Hospital stay days	
	Correlation coefficient	Correlation significance
SIRS_score_t0	.553	.000
SIRS_score_t1	.522	.000
SIRS_score_t2	.436	.001

Table 1. Correlation of duration of the hospital stay days with SIRS score

Variable	Treatment outcome	
	Correlation coefficient	Correlation significance
SIRS_score_t0	-.247	.057
SIRS_score_t1	-.240	.065
SIRS_score_t2	-.250	.054

Table 2. Correlation of the treatment outcome with SIRS score

16,524; t₁=-10,407; t₂=-9,842, p < 0,05). There is a statistically significant difference in the pCO₂ values in all stages between groups (c²: t₀=2,582; t₁=1,678; t₂=1,162, t: t₀=4,323; t₁=2,653; t₂=2,229, p<0,05). Analyzing the differences between value of the parameters during stages (t₀, t₁, and t₂), Wilcoxon paired t-test showed that there was statistically significant difference in the number of leukocytes in all stages for both groups of subjects. The largest leukocytes count for the elective surgery group was in t₁, and in the non-elective surgery group in t₀. Statistically significant difference in the number of leukocytes between groups was in t₀ (p < 0001). An analysis of the parameters that represent the extent of the body's inflammatory response has shown that systemic inflammatory response occurs after both elective and non-elective surgery, but with a statistically significant difference in its incidence. Elective surgery group had a low incidence of systemic inflammatory response of the body (Figure 1), as opposed to a non-elective surgery group, with high incidence (p < 0.0001) (Figure 2).

The SIRS score has a good positive correlation with the length of treatment, while the correlation with the out-

come of treatment has no statistical significance (Table 1 and 2).

4. DISCUSSION

The acute phase reaction of the body is a complex series of reactions that begin in response to infection, physical trauma or malignancy, and is characterized by leukocytosis, elevated body temperature, changes in the metabolism of many organs, and the change in the concentration of various acute phase proteins in plasma (7).

Early systemic leukocytosis appears due to surgical stress. The increased release of cortisol as the body's response to stress or administration of adrenaline during major surgical procedures also affects the increase in the number of leukocytes (8, 9). Hong (10) published the results of a study that analyzed changes in the number of leukocytes in patients who underwent laparoscopic surgery due to endometriosis comparing preoperatively administration of ketorolac vs placebo. Preoperative ketorolac reduced postoperative pain and influenced the WBC response. In our study, the non-elective surgery group subjects had an increase in the leukocytes count in t_0 , while in the elective surgery group subjects this increase is seen in t_1 . In the non-elective surgery group there is a gradual decline in the leukocytes count in t_1 , but it is still above the upper limit, with the tendency of decreasing in t_2 when it is within the reference range. In t_1 for the elective surgery group, the increased number of leukocytes is lower than the increased number of leukocytes for the non-elective surgery group, but without a statistically significant difference, with the tendency further decreasing to t_2 when it is at the reference range and lower than in subjects from non-elective surgery group. Therefore, in non-elective surgery group inflammatory reaction caused by the condition for which the surgical procedure is indicated, leads to an increase in the number of leukocytes, which gradually decreases during recovery time, because the root cause is eliminated, and it has been cleared up with an operative procedure. Changes of the leukocytes count were proportional to the changes of the neutrophils count. Numerous studies have shown that elevated body temperature is a frequent sign of the first and second postoperative day in large operative procedures, mostly caused by an inflammatory stimulus of surgery (11, 12, 13). Wortel et al. (14) reported that the postoperative level of IL-6 is directly proportional to the value body temperature. Other studies have shown that the risk of postoperative temperature is greater with a larger operative procedure (15). In our study, in elective surgery group there was no increase in body temperature at any stage of the examination. Non-elective surgery group had an elevated temperature at all stages, and the highest in t_0 with a downward trend after elimination of the cause of inflammation by surgery. The value of the body temperature of our subjects is well correlated with the leukocyte count.

In our study, elective surgery group had a lower heart rate than non-elective surgery group. Elective surgery group subjects came prepared for surgery. The stress stimulus that triggers the response of the organism is

only a surgical procedure, and due to the activation of the sympathetic nervous system, there is a significant difference in heart rate in t_1 . However, non-elective surgery group subjects were hospitalized due to acute abdomen and that had already triggered the stress response, and they had tachycardia in t_0 . The operative procedure is the cause of stress to body, but also removes the stimulus that has already triggered the inflammatory reaction in the non-elective surgery group subjects; therefore we had lower values of the heart rate in t_1 and t_2 . Saha and associates (16) published the results of a study that analyzed hemodynamic changes in subjects undergoing surgery of the upper abdomen. They reported that preoperative administration of low dose propranolol stabilizes hemodynamic changes caused by surgical trauma.

Activation of the sympathetic nervous system during the stress response of the body and the emergence of the so-called hyper adrenergic condition do not only causes hemodynamic changes—hypertension and tachycardia, but also causes the hyperventilation. Tachypnea may be a reflection of increased metabolic stress during inflammation or infection, but may also be a threatening sign of inadequate perfusion that results in anaerobic cell metabolism (17). The cause of tachypnea in the inflammatory response of the organism depends on the intensity and duration of action of the stress agent, as well as the activation and ability of the compensatory mechanisms of the organism to neutralize the action of the stress stimulus. If the stress stimulus is low to moderate intensity, with shorter action and with compensatory mechanisms sufficient to neutralize the effect of the stress stimulus, then tachypnea is mainly a reflection of the so-called hyper adrenergic condition. With more potent long acting stress agent, due to poor perfusion of the peripheral tissues, anaerobic metabolism starts to produce acid products with a stimulating effect on the respiratory center. In our study, elective surgery group subjects were not in hypocapnia at any stage of the study, as opposed to non-elective surgery group subjects in whom the lowest value of pCO_2 was recorded in t_0 with the gradual increase in t_1 and t_2 . Hypocapnia in this group of subjects may be a reflection of a hyper adrenergic condition but also a sign of weaker perfusion, since the surgery eliminate the primary cause of the inflammatory cascade, hydration improves perfusion, PCO_2 values increases, but are still under reference range. Surgical procedure induces the onset of an inflammatory cascade and the release of inflammatory cytokines. Laparoscopic surgery reduces both local and systemic production of cytokines and acute-phase reactants, and preserves better the peritoneal immune ability compared to open surgical procedures (18). If it persists the action of the stress stimulus from damaged tissue with addition of action of another stress stimulus, the local response transforms into the systemic reaction of the organism known as the systemic inflammatory response of the organism (19). SIRS is a serious condition characterized by systemic inflammation leading to organic dysfunction, sometimes several organ systems. It is a form of cytokine storm, with an abnormal regulation of different cytokines. Criteria confirming the

systemic reaction of the organism to the action of stress stimulus were established in 1992 at the Conference of the American College of Thoracic Doctors and the Association of Intensive Medicine and since then have been used in clinical practice. Takenaka and associates (20) published the results of study showing that postoperative monitoring of the parameters of the acute phase (IL-6 and CRP) and the parameters of SIRS is very significant, because they correlate well with the intensity of surgical stress and length of hospitalization. The Hague et al. (21) investigated the appearance of SIRS and multiorgan dysfunction in patients who underwent gastrointestinal surgery. The results showed that the length of the SIRS or the number of positive SIRS criteria after surgery significantly correlated with the parameters of surgical stress (blood/weight loss, duration of operation) and CRP value. The SIRS that continued or reappeared after the third postoperative day was an early sign of postoperative complications. They concluded that SIRS is a useful criterion for recognizing postoperative complications and organic dysfunction. Becher et al. (22) published the results of a study, in which they investigate the effect of an inflammatory response on the outcome of treatment for patients undergoing emergency surgery in the colorectal area. They concluded that the impossibility of regulating the systemic inflammatory response of the organism was the primary cause of the death of non-elective surgery group subjects, and patients with SIRS or sepsis in whom the surgical procedure lasted less than 2.5 hours had less postoperative complications. Their results further reinforce the concept of the importance of surgical intervention in the right time with the best possible control of tissue manipulation, which potentially reduces inflammation. In our study, significantly more incidence of SIRS score had non-elective surgery group subjects, preoperatively (86.7%), with a tendency of gradual decrease in the next stages of the study (60% in t_1 and 40% in t_2). The preoperatively high incidence of SIRS score is a result of the already launched inflammatory reaction. The postoperative incidence is still high and gradually decreases as the root cause of the inflammatory response is resolved, but its residual effects are interpose with the effect of the performed surgery procedure, as a stress stimulus. Positive SIRS criteria are a postoperative reflection of a triggered inflammatory cascade, but with a tendency to settle. The SIRS score of our subjects correlates well with the duration of hospitalization, and somewhat weaker with the outcome of treatment. A weaker correlation with the outcome of treatment is explained by settling the inflammatory cascade within 72 hours. It is likely that we would have a better correlation, if the SIRS parameters were monitored after this period.

5. CONCLUSION

The surgical procedure triggers the inflammatory reaction of the organism, which is manifested by the change of the parameters of the inflammation. Elective surgery procedures are characterized by a localized inflammatory reaction, whereas patients, who are operated due to an acute surgical condition, have a high incidence of sys-

temic inflammatory response to the organism. Monitoring inflammation scores in surgical patients is important for analyzing of the success of surgical treatment. By modifying the therapy and influencing to the inflammatory response, the results of treatment are improved.

- **Conflict of interest:** none declared.
- **Author contribution** J.S. made substantial contribution to conception and design, acquisition of data, analysis and interpretation of data, drafted the article, critically revised the article for important intellectual content and approved final version to be published. L.R.T. made substantial contribution to analysis and interpretation of data. S.H. drafted the article. S.S.A. and S.H. made substantial contribution to acquisition of data.

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