ORIGINAL ARTICLE

Relationship between SIRI, SII values, and Alvarado score with complications of acute appendicitis during the COVID-19 pandemic

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ABSTRACT

BACKGROUND: The aim of the study was to investigate the clinical variations of Systemic Inflammatory Response Index (SIRI), Systemic Inflammation Index (SII), and Alvarado Score during the COVID-19 pandemic period.

METHODS: Between March 2019 and March 2021, 161 consecutive patients who had surgery due to acute appendicitis were retrospectively recruited from Trakya University in Edirne, Turkey. Group I included patients who had surgery during the COVID-19 pandemic and Group II included patients who had surgery before the COVID-19 pandemic period. A total of 80 patients volunteered for Group I and 81 patients for Group II. The neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio, and lymphocyte/monocyte ratio were calculated. SII was calculated by the formula: platelet (P) × neutrophil (N)/lymphocyte (L). NLR was calculated by dividing the neutrophil count by the number of lymphocytes. SIRI was defined as follows: SIRI = (neutrophil × monocyte/lymphocyte). The Alvarado score was also calculated by using patient history, clinical examination, and laboratory findings.

RESULTS: There was a significant difference between the two groups in terms of displacing pain, nausea/vomiting, right lower quadrant tenderness, rebound, hyperthermia, leukocytosis, and total Alvarado score ($p<0.001$). There was a significant difference between two groups in comparison of C-reactive protein, SIRI, and SII values ($p<0.001$). Group I patients had higher values of these parameters than Group II.

CONCLUSION: Based on the results obtained from this study, we conclude that COVID-19 pandemic has caused an increase in patients with acute appendicitis admitted to the hospital. This late diagnosis of acute appendicitis caused more complications during COVID-19 pandemic. Alvarado score, SIRI, and SII can be used as a marker to indicate whether complications of acute appendicitis occurred pre- or post-operatively. Therefore, Alvarado score, SIRI, and SII are directly proportional to the complication of acute appendicitis.

Keywords: Akut appendicitis; Alvarado; COVID-19; SII; SIRI.

INTRODUCTION

Acute appendicitis is one of the most common diseases that often results in emergency operation. The lifetime occurrence of this disease is approximately 7%, with a perforation rate of up to 20%.[1] Acute appendicitis is diagnosed mainly by the help of the medical history and clinical examination. In addition, laboratory investigations also may be helpful for diagnosis (such as white blood cells [WBCs] count or C-reactive protein [CRP] level). Alvarado scoring system, which was introduced in 1986, is one of these systems and is based on history, clinical examination and laboratory findings.[2] Imaging modalities are not requested routinely because they have been shown to add very little information unless there are complications. The definitive diagnosis is achieved during surgery and following histopathologic examination of the resected appendix.[3]

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Any failure to diagnose acute appendicitis can result in delay of the surgical treatment, which results in many complications such as perforation, abscess and sepsis. Therefore, the delay in diagnosis means that increasing morbidity and mortality for acute appendicitis patients.[4]

From the moment of its discovery in December 2019, coronavirus disease 2019 (COVID-19) infections began a rapid exponential growth. On March 11, 2020, the World Health Organization declared the outbreak a global pandemic.[5] The unprecedented global crisis resulting from the coronavirus pandemic imposed a large burden on medical systems worldwide. As a result of this, there has been a decrease in hospital visits of patients who complain of acute abdominal symptoms. Because of this delay in emergency rooms visits, there was a lower ratio of acute abdomen cases and a higher ratio of complicated surgical cases observed worldwide by the surgeons during the COVID 19 pandemic.

The systemic inflammatory response index (SIRI), which is usually evaluated based on peripheral blood-based parameters, (e.g., lymphocytes, C-reactive protein, monocytes, neutrophil, or platelet count) has been reported to independently associate with oncologic outcomes in various cancers.[6,7] SIRI is calculated by (N×M)/L, where the N, M, and L represent neutrophil, monocyte, and lymphocyte counts, respectively. Several of these parameters have been converted to ratios, such as the neutrophil to lymphocyte ratio (NLR),[8] platelet to lymphocyte ratio (PLR),[9] and lymphocyte to monocyte ratio (LMR),[10] which have been broadly found to be important prognosis predictors. SIRI is usually associated with oncologic diseases in many studies; however, there is no study to evaluate the SIRI for the acute appendicitis.

Systemic immune-inflammation index (SII) is calculated by (N×P)/L, where N, P, and L represent neutrophil, platelet, and lymphocyte counts, respectively. SII is associated with some malignant tumors such as metastatic renal cell cancer and metastatic castration resistant prostate cancer.[11] Compared with the biomarkers of NLR, LMR, and PLR, the SII may comprehensively reflect the balance between the host immune and the inflammatory condition.

We aimed to evaluate the local impact of the COVID 19 pandemic on the emergency presentation of acute appendicitis by comparing SIRI, SII, and Alvarado score in Trakya University Hospital.

MATERIALS AND METHODS

Patients

This study was approved by the local Ethics Committee of the Trakya University, Edirne, Turkey. Written informed consent was obtained from each participant in accordance with the institutional guidelines. Between March 2019 and March 2021, 161 consecutive patients who had surgery because of acute appendicitis were retrospectively recruited from the Trakya University, Edirne, Turkey. The inclusion criteria for this study were as follows: Must be 18 years of age and older, must have diagnosis of acute appendicitis with the histopathological examination, and no history of any malignant or hematologic disorders. Patients in this study were managed by surgical treatment. We have two groups according to operation date: Group I included patients who had surgery during the COVID-19 pandemic and Group II included patients who had surgery before the COVID-19 pandemic. We have 80 patients in Group I and 81 patients in Group II. We compared complications and inflammatory markers between these two groups. Laparoscopic or open appendectomy was applied randomly to the patients.

Laboratory Tests

Routine laboratory measurements, including WBC count, neutrophil, lymphocyte, monocyte, and platelet count as well as serum albumin and CRP, were performed before conducting the acute appendicitis diagnostic interventions or treatment. The NLR, PLR, and LMR were calculated. SII was calculated by the formula: platelet (P)×neutrophil (N)/lymphocyte (L). NLR was calculated by dividing the neutrophil count by the number of lymphocytes. SIRI was defined as follows: SIRI = (neutrophil × monocyte)/lymphocyte).

Statistical Analysis

A Normal distribution range was controlled by the Shapiro–Wilk test. A Mann–Whitney U test was used for variations that are contrary to the normal distribution range in the comparison of two groups. The relations between qualitative variations were analyzed by Pearson Chi-square test and Fisher's accurate test. Median and quartile values were used for the quantitative variations, and percentage and frequency rates were given for the qualitative variations as descriptive statistical evaluations. $P<0.05$ was determined to be significant for the all statistical analysis. All statistical analyses were performed using TURCOSA (Turcosa Analytics Ltd Co, Turkey, www.turcosa.com.tr) statistical software program.

RESULTS

In this study, we have two groups: Group I includes the 80 patients who were operated because of acute appendicitis during the COVID-19 pandemic, from March 2020 to March 2021 and Group II includes the 81 patients who were operated because of acute appendicitis before the COVID-19 period from March 2019 to March 2020.

The mean age for Group I was 32 (range [min:max], 22.3:45] and for Group II is 35 (range [min:max], 25.5–55.5). There is no significant difference between these two groups according to age ($p=0.124$). Furthermore, there was no significant difference between two groups according to gender (Table 1).

Table 1. Comparison of age and gender between two groups

	Group I	Group II
Age	32 (22.25–45)	35 (25.5–55.5)
Male, n (%)	55 (68.7)	46 (56.7)
Female, n (%)	25 (31.2)	35 (43.2)

Table 2. Comparison of surgical technique and perforation rate between two groups

	Group I	Group II	p-value
Laparoscopic	46.2%	81.8%	<0.001
Perforation	46.1%	11.1%	<0.001

Table 3. Comparison of Alvarado score parameters between two groups

	Group I	Group II	p-value
Displacing pain	52.5%	22.2%	<0.001
Loss of appetite	31.2%	19.7%	0.094
Nausea/Vomiting	46.2%	8.6%	<0.001
Right lower quadrant tenderness	96.2%	81.4%	0.003
Rebound	80%	54.3%	<0.001
Hyperthermia	38.7%	7.4%	<0.001
Leukocytosis	92.2%	65.4%	<0.001
Neutrophilia	88.7%	86.4%	0.478
Total Alvarado Score	8 (7–9)	6 (5–7)	<0.001

Table 4. Comparison of inflammatory parameters between the two groups

	Group I	Group II	p-value
CRP	45.4 (10.7–84.6)	7.7(5.8–32.4)	<0.001
NLR	7.3 (4.7–10.9)	5.6 (3.2–11.2)	0.097
PLR	169.9 (125.4–214.3)	131 (101.7–237.1)	0.104
LMR	1.65 (1.11–2.53)	2.08 (1.23–3.5)	0.099
SIRI	7.8 (4.1–10.9)	4.3 (2–10)	<0.001
SII	2.235 (1.155–2.887)	1.180 (820–2.256)	<0.001

CRP: C-reactive protein; NLR: Neutrophil to lymphocyte ratio; PLR: Platelet to lymphocyte ratio; LMR: Lymphocyte to monocyte ratio; SIRI: Systemic inflammatory response index; SII: Systemic immune-inflammation index.

There was a significant difference between the two groups in terms of surgical technique and perforation rate (Table 2). There was a significant difference between the two groups in terms of displacing pain, nausea/vomiting, right lower quadrant tenderness, rebound, hyperthermia, leukocytosis, and total Alvarado score. On the other hand, there was no significant difference between two groups in terms of loss of appetite and neutrophilia (Table 3).

The mean CRP value in Group I was 45.4 (10.7–84.6) and in Group II was 7.7 (5.8–32.4) (p<0.001). The mean NLR value in Group I was 7.3 (4.7–10.9) and in Group II was 5.6 (3.2–11.2) (p=0.097). The mean PLR value in Group I was 169.9 (125.4–214.3) and in Group II was 131 (101.7–237.1) (p=0.104). The mean LMR value in Group I was 1.65 (1.11–2.53) and in Group II was 2.08 (1.23–3.5) (p=0.099). The mean SIRI value in Group I was 7.8 (4.1–10.9) and in Group II was 4.3 (2–10) (p<0.001). The mean SII value in Group I was 2235 (1,155–2,887) and in Group II was 1180 (820–2,256) (p<0.001). There was a significant difference between the two groups in terms of SIRI and SII values (Table 4).

DISCUSSION

Acute appendicitis is one of the most common diseases that require emergency surgery. Anamnesis, clinical, and physical examinations play main role for the diagnosis of acute appendicitis. In addition, laboratory tests and radiologic imaging techniques can be helpful for definitive diagnosis. Alvarado score system is non-invasive, safe, simple, reliable, and repeatable diagnostic method.[12]

In a study by Canbak and Acar, displacing pain was found in 91.4%, tenderness in the right lower quadrant in 82.8%, loss of appetite in 78.5%, and nausea/vomiting in 61.4% of the patients.[12] On the other hand, displacing pain was found 52.5 of Group I and 22.2% of Group II, right lower quadrant tenderness in 96.2% of Group I and 81.4% of Group II, loss of appetite in 31.2% of Group I and 19.7% of Group II, nausea/vomiting in 46.2% of Group I, and 8.6% of Group II in our study. We conclude that these physical and clinical examination findings were found at a higher rate in Group I than the Group II. The Alvarado score was classified in two groups by Canbak and Acar based on the higher/lower score of 7. We found that Group I had a higher Alvarado score than Group II in our study. Therefore, these findings suggest that, during the COVID-19 pandemic, clinical and physical examination findings were worsened because of late presentation to the hospital.

Lee-Archer et al.[13] compared the complication rates of acute appendicitis in the COVID-19 pandemic and corresponding period. Complication rate was 47.9% in during the COVID-19 pandemic and 24.6% in the before the pandemic in their study. The complication rate in COVID-19 period was significantly higher than the corresponding period. In our study, we compared the perforation rates as a complication of acute appendicitis. In Group I, perforation rate was 46.1% and 11.1% in Group II. There was also a significant difference in complication rate between the two groups same as the study by Lee-Archer et al.[13]

Orthopoulos et al.[14] also compared the complication rates and treatment modalities of acute appendicitis between the pandemic and non-pandemic period. They found out that laparoscopic appendectomy rate was 97% for the non-pandemic period and 87% for the pandemic period. In our study, the laparoscopic appendectomy rate was 81.8% in Group II and 46.2% in Group I. There may be two causes for the higher rate of open appendectomy during the COVID-19 pandemic. First, the higher rate of complication may cause a difficult exploration laparoscopically. Second, the preference of surgery due to the high risk of COVID-19 infection related to breathing of abdominal gas during laparoscopic surgery.

Inflammatory markers such as NLR, PLR, LMR, SIRI, and SII have been used to evaluate the prognosis of breast cancer.[15,16] They have shown that these inflammatory parameters were associated with poor prognosis of breast cancer but the mechanism was unclear. Another study by Chen et al.[17] showed that SIRI might serve as an independent prognostic predictor, and it could be used to better predict the prognosis in patients with localized or locally advanced clear cell renal cell carcinoma. In another study by Wang and Zhu,[18] the prognostic value of SII for gastric cancer was evaluated. They showed that SII may serve as a convenient, low-cost, and non-invasive prognostic marker for patients following radical operation for carcinoma of stomach in gastric cancer. Chen et al.[19] showed that elevated SII was correlated with poor OS and recurrence in patients with CRC. They stated that SII was a superior prognostic factor for survival outcome compared to NLR and PLR. In our study, we evaluated CRP, LMR, PLR, NLR, SII, and SIRI between the two groups. There was no significant difference in NLR, PLR, and LMR values between groups. CRP, SIRI, and SII values in Group I was significantly higher than the Group II ($p<0.001$). Therefore, CRP, SII, and SIRI can be used as a marker to know about the complications of acute appendicitis preoperatively.

Conclusion

Based on the results obtained from our study, we conclude that the COVID-19 pandemic has caused a late presentation of patients to the hospital. The late diagnosis of acute appendicitis caused more complications during COVID-19 pandemic. Alvarado score, SIRI, and SII can be used as a marker to determine whether the complications of acute appendicitis would occur pre- or post-operatively. Therefore, Alvarado score, SIRI, and SII are directly proportional to the complication of acute appendicitis. A prospective study may give more information about the relationship of these markers with the clinical situation of acute appendicitis such as complications, hospital stay, and treatment modalities.

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ORİJİNAL ÇALIŞMA - *ÖZ*

COVID-19 pandemisi süresince SIRI, SII ve Alvarado skorlarının akut apandisit komplikasyonlarıyla olan ilişkisi

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AMAÇ: COVID-19 pandemisi süresince SIRI (Systemic Inflammatory Response Index), SII (Systemic Inflammation Index) ve Alvarado skorlarında oluşan değişiklikleri araştırmak.

GEREÇ VE YÖNTEM: Mart 2019 ile Mart 2021 tarihleri arasında Edirne Trakya Üniversitesi'nde akut apandisit nedeniyle ameliyat edilmiş olan 161 ardışık hastanın dosyaları geriye dönük olarak değerlendirildi. Grup I'deki hastalar COVID-19 pandemi sürecinde ameliyat olan hastalardan oluşurken, Grup II'deki hastalar pandemik süreci öncesinde ameliyat olan hastalardan oluşmaktadır. Grup I'de 80, Grup II'de 81 hasta bulunmaktadır. Nötrofil/lenfosit (NLR), trombosit/lenfosit (PLR) ve lenfosit/monosit (LMR) oranları hesaplandı. SII değeri (trombosit x nötrofil/lenfosit) formülü kullanılarak, SIRI değeri ise (nötrofil x monosit/lenfosit) formülü kullanılarak hesaplandı. Alvarado skoru ise hasta öyküsü, klinik muayene ve laboratuvar bulguları kullanılarak hesaplandı.

BULGULAR: Yer değiştiren ağrı, bulantı/kusma, sağ alt kadran ağrısı, rebound, yüksek ateş, lökositoz ve toplam Alvarado skorları değerlendirildiğinde iki grup arasında belirgin fark saptandı ($p<0.001$). Aynı zamanda iki grup arasında CRP, SIRI ve SII değerleri arasında belirgin farklılık oluğu görüldü ($p<0.001$). Bu parametrelerin hepsinde Grup I'deki değerler Grup II'ye göre daha yüksek saptandı.

TARTIŞMA: Çalışmamızdan elde ettiğimiz verilere dayanarak COVID-19 pandemi sürecinde akut apandisit nedeniyle hastaneye başvuran hasta oranında artış olduğu görüldü. Bununla birlikte COVID-19 pandemi sürecinde geç tanı alınması nedeniyle akut apandisit komplikasyonları daha fazla görülmüştür. Akut apandisit hastalarında ameliyat öncesi veya sonrası komplikasyonları göstermede Alvarado skoru, SIRI ve SII bir belirteç olarak kullanılabilir. Aynı zamanda Alvarado skoru, SIRI ve SII değerlerinin akut apandisit komplikasyonları ile orantılı olarak değişkenlik gösterdiği görüldü.

Anahtar sözcükler: Akut appendisit; Alvarado; COVID-19; SII; SIRI.

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