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The Comparison of Clinical Features Between Patients with Positive and Negative Appendectomy

Pozitif ve Negatif Apendektomi Yapılan Hastaların Klinik Özelliklerinin Karşılaştırılması

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Abstract

Aim: The objective of this study was to retrospectively compare clinical features and prognostic values between the patients who were referred to the general surgery clinic of our hospital with the presumed diagnosis of acute appendicitis and underwent positive or negative appendectomy.

Methods: Patients were divided into two groups as positive (n:362) and negative appendectomy (n:284) and the data obtained were compared between these two groups. Laboratory investigations were performed in all patients, and white blood cell, mean platelet volume (MPV), neutrophils count, neutrophils (%) (NEU%), C-reactive protein and total bilirubin (TBIL) values were studied.

Results: The mean CRP value was found as 57.68 in positive appendectomy (PA) group and 41.43 in negative appendectomy (NA) group, and the mean CRP value was statistically significantly higher in PA group, compared to NA group. The mean TBIL value was 0.97 mg/dl in PA group and 0.69 mg/dl in NA group, and the mean TBIL value was statistically significantly higher in PA group. The other parameters were similar between the groups.

Conclusion: According to the results of our study, CRP and TBIL values significantly differ between positive and negative appendectomy patients. Therefore, these values may be used as specific biomarkers in predicting positive acute appendicitis.

Key Words: Appendicitis; appendectomy; C-Reactive Protein; bilirubin; mean platelet volume

Özet

Giriş : Bu çalışmanın amacı, hastanemiz genel cerrahi kliniğine başvuran ve ön tanıda akut apandisit düşünülerek pozitif veya negatif apendektomi yapılan hastaların klinik özelliklerini ve prognostik öneme sahip olabilecek parametreleri retrospektif olarak karşılaştırmaktır.

Yöntem : Hastalar pozitif (n: 362) ve negatif apendektomi (n: 284) olarak iki gruba ayrıldı ve elde edilen veriler bu iki grup arasında karşılaştırıldı.Tüm hastalarda laboratuvar incelemeleri yapılarak lökosit, ortalama trombosit hacmi (MPV), nötrofil sayısı, nötrofil (%), C-reaktif protein (CRP) ve total bilirubin (TBIL) değerleri analiz edildi.

Bulgular : Ortalama CRP değeri pozitif apendektomi (PA) grubunda 57.68 ve negatif apendektomi (NA) grubunda 41.43 olarak bulundu ve ortalama CRP değeri NA grubuna göre PA grubunda istatistiksel olarak daha yüksek saptandı. Ortalama total bilirübin değeri PA grubunda 0.97 mg / dl, NA grubunda 0.69 mg / dl idi. PA grubunda istatistiksel olarak anlamlı yüksekti. Diğer laboratuar özellikler açısından iki grup arasında anlamlı fark saptanmamıştır.

Sonuç: Çalışmamızın sonuçlarına göre, CRP ve total bilirübin değerleri pozitif ve negatif apendektomi hastaları arasında anlamlı farklılık göstermektedir. Bu nedenle bu değerler, pozitif akut apandisiti tahmin etmede spesifik biyolojik belirteçler olarak kullanılabilir.

Anahtar Kelimeler : Apandisit; apendektomi; C-reaktif protein; bilirubin; ortalama trombosit hacmi

Introduction

Appendicitis is the most common emergency surgery, with a lifetime risk for appendicitis estimated as 8.6% in men and 6.7% in women (1). In Europe, 112/100000 persons present to emergency departments each year due to acute appendicitis (2). The rate of morbidity from acute appendicitis has been reported between 7%-16% in the general population (3). Appendicitis usually presents with anorexia and tenderness in the right lower abdominal quadrant. However, pain in the right lower quadrant can be associated with numerous pathologies. Because of the wide spectrum of differential diagnosis and lack of specific markers for appendicitis, preoperative diagnosis of this disease is quite challenging (4). Today, the incidence of appendicitis is increasing in developing countries (5). Since serious complications may occur in the case of delayed diagnosis, prompt action is necessary. The management of appendicitis focuses on the prevention with a timely intervention before an uncomplicated appendicitis progresses to a complicated one. Appendectomy, which is sometimes performed on a normal appendicitis is

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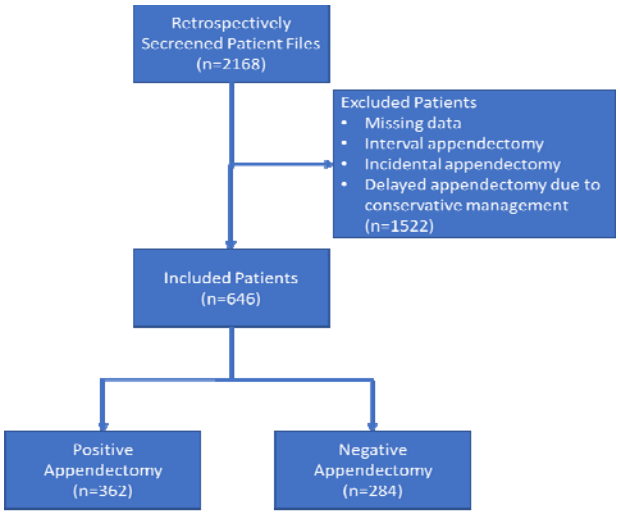
known as "negative appendectomy" (NA) (6). Complications of acute appendicitis include perforation, peritonitis and sepsis (7). This can increase the rate of negative appendectomy operations. Negative appendectomy rate (NAR) is defined as the incidence of removing appendices that are pathologically normal (8). Negative appendectomy leads to prolonged hospitalization, morbidity and increased costs due to uncesessary operations. In addition, negative appendectomy may be associated with severe postoperative complications. Therefore, an accurate preoperative diagnosis is essential in the cases of suspected acute appendicitis. In the United States of America (USA) over 250000 appendectomy operations are performed yearly, and the rate of negative is approximately 15% in these operations (9). However, owing to better imaging modalities, a constant decrease is seen in the rate of Nas (10). Gynecological pathologies in female patients in childbearing period mimic acute appendicitis, which can cause an increase in the rate of negative Nas (11). According to the current guidelines, the diagnosis of acute appendicitis is established according to clinical examination and confirmed with imaging investigations and some biomarkers including WBC count and CRP (12). Computed tomography (CT) and ultrasonography are used as imaging modalities in order to set a more accurate diagnosis. The objective of this study was to retrospectively compare clinical features and prognostic values between the patients who were referred to the general surgery clinic of our hospital with the presumed diagnosis of acute appendicitis and underwent positive or negative appendectomy.

Material and Methods

Data of a total of 2168 patients who were referred to our general surgery clinic with the presumed diagnosis of appendicitis and underwent appendectomy between 2010 and 2019 were retrospectively evaluated. Among these patients, 1522 were excluded from the study because of missing data, and those who underwent interval appendectomy, and incidental appendectomy, and the patients for whom appendectomy operation was delayed due to conservative treatment. Finally, data of 646 patients were obtained and evaluated. Patients aged between 16–90 years. Patients were divided into two groups as positive (PA) (n:362) and negative appendectomy (NA) (n:284) and the data obtained were compared between these two groups (Flowchart 1).



Flowchart 1. Study population

Patients' demographic data such as age and gender, date and type of operations, investigations, clinical presentation, macroscopic and microscopic findings, imaging and pathological findings were recorded and analyzed. In addition, laboratory investigations were performed in all patients, and white blood cell (WBC), mean platelet volume (MPV), neutrophils count (NEU), neutrophils (%) (NEU%), C-reactive protein (CRP) and total bilirubin (TBIL) values were studied. Inclusion criteria included all patients operated during the nine years period. Considering clinical conditions of the patients and in the cases of uncertain diagnosis or where the clinical picture did not meet physical findings (age, pregnancy, having gynecological examination, comorbidities etc.) abdominopelvic computed tomography and ultrasonography examinations were performed in some patients. The diagnosis of appendicitis was established based on macroscopic findings. Histological diagnosis of appendicitis was set according to the infiltration of muscularis propria with neutrophils granulocytes. Appendectomies were performed by conventional or laparoscopic methods. Lack of the appendicitis in the pathology reports was considered negative appendectomy. In order to identify appendectomy cases with negative samples, pathology reports were interpreted by an author blinded to whether preoperative imaging was performed. Negative appendectomy was defined as a normal appendix following the resection due to suspected appendicitis or medically unnecessary appendectomy. Medically unnecessary appendectomy was defined as an appendectomy operation performed in the case of typically contraindicated surgery.

Table 1: Frequency distribution of patients' gender and age by type of appendectomy

	PA. (n=362)		NA. (n=284)	
	n	%	n	%
Male	226	62.4	134	47.2
Female	136	37.6	150	52.8
Sum	362	100	284	100
Mean Age	28.2 ±16.65		31.9±17.4	

PA: Positive appendicitis, NA: Negative appendicitis

Table 2: Comparison results of WBC, MPV, NEU (%), NEU, CRP and TBIL parameters of patients according to the type of appendectomy

	Appendectomy Type	n	$\bar{x}$	SD	t	P
WBC	Positive	362	9.97	3.44	1.81	0.070
	Negative	284	9.51	2.96		
MPV	Positive	362	7.88	1.65	-1.55	0.120
	Negative	284	8.09	1.79		
NEU%	Positive	362	76.01	12.94	.31	0.750
	Negative	284	75.69	12.23		
NEU	Positive	362	7.33	2.72	-.69	0.480
	Negative	284	7.50	3.64		
CRP	Positive	362	57.68	58.92	3.54	0.000
	Negative	284	41.43	56.36		
TBIL	Positive	362	0.97	0.57	7.39	0.000
	Negative	284	0.69	0.39		

Ethical approval was obtained from the local ethics committee of Sakarya University before starting the study with the 27/07/2020 dated and E.6712 numbered decision. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Statistical analysis: Data obtained in the study were analyzed utilizing SPSS version 23.0 (Statistical Package for Social Sciences, SPSS, IBM Incusing Chicago, IL, USA) statistical package software. Normality of the variables was analyzed with the Kolmogorov-Smirnov test. In the comparison of the variables between the groups, Independent Student t test among was used for the normally distributed variables, and Mann-Whitney U test for non-normally distributed variables. Continuous variables were expressed with mean ± standard deviation, while categorical variables were given as frequency and percentage. $p < 0.05$ values were considered statistically significant.

Results

A total of 646 patients were included in the study with 362 (56%) being in PA group and 284 (44%) in NA group. Of all patients included in the study, 360 (55.7%) were male and 286 (44.3%) were female. A total of 226 (62.4%) patients were male and 136 (37.6%) were female in PA group. Whereas 134 (47.2%) were male and 150 (52.8%) were female in the NA group. No statistically significant difference was seen between both groups in terms of gender. The mean age of all patients was 30.1 ± 16.9 years, and the mean age was found as 28.2 ± 16.65 years in PA group and 31.9 ± 17.4 years in NA group. There was no statistically significant difference between PA and NA groups in terms of age. Appendectomies were

performed with laparoscopic method in 199 (54.9%) of the patients in PA group and in 207 (72.8%) of the patients in NA group. The remaining patients underwent open surgery. When status of having gynecological examination was examined among the female patients; 105 (77.3%) female patients in PA group and 125 (83.5%) female patients in NA group underwent gynecological examination. Demographic features of the patients are shown in Table 1. Laboratory outcomes were examined and compared between the two groups. Accordingly, the mean WBC value was found as 9.97 K/mm^3 in PA group and 9.51 K/mm^3 in NA group, and there was no statistically significant difference between both groups (p=0.07). The mean MPV value was found as 7.88 fl in PA groups and 8.09 fl in NA group, and there was no statistically significant difference between both groups (p=0.12). NEU (%) value was found as 76.01 in PA group and 75.69 in NA group. No statistically significant difference was observed between the two groups in terms of the mean NEU (%) value (p=0.75). The mean neutrophil count was found as 7.33 K/mm3 in the PA group and 7.50 K/mm3 in NA group, and no statistically significant difference was found between the two groups (p=0.48). The mean CRP value was found as 57.68 mg/dl in PA group and 41.43 mg/dl in NA group. There was a statistically significant difference between both groups in terms of the mean CRP value (p = 0.01). When total bilirubin values were examined; the mean TBIL value was 0.97 mg/dl in PA group and 0.69 mg/dl in NA group, and the mean TBIL value was statistically significantly higher in PA group (p = 0.01) (Table 2). When diameters of appendicitis were evaluated; the mean appendicitis diameter was found as 1.09 cm in PA group and 0.88 cm in NA group, and the mean appendicitis diameter was statistically significantly higher in PA group compared to NA group (p = 0.01).

Discussion

Surgical intervention of a normal appendicitis exposes patients to unnecessary anesthesia and surgical complications, and this may be resulted from improper clinical evaluation, and lack of diagnostic methods. Despite the high incidence of acute appendicitis and use of laboratory markers and imaging modalities, the accurate diagnosis remains challenging. Research of the diagnostic process used for acute appendicitis is highly dynamic, within this context information such as novel inflammatory biomarkers is constantly reported in the literature (13). As in our country, high rates of appendicitis cases have been reported in some other countries (14). Therefore, more effort should be made in order to reduce the incidence of NAR and its complications on patients and hospitals (15). Negative appendectomies lead to both postoperative complications, increased morbidity and mortality rates and costs. Thus, investigation of the factors leading to negative appendectomies is of paramount importance. Among these factors, laboratory parameters take an important place. However, to our knowledge there is no consensus in the literature on this subject. In our study, we first evaluated laboratory values between positive and negative appendectomy cases. We performed preoperative computed tomography by excluding elderly patients, pediatric patients and those with comorbidities. We observed that the rate of negative appendectomy was lower in patients who underwent CT (24.3%). In a study by Wagner et al., the rate of performing preoperative CT raised to 95% from 32% within 10 years (16). In our study, 84.6% of female patients were found to have a gynecological examination. In a study by Joshi et al. 57.1% of female patients were reported to have gynecological examination (15). We believe that higher gynecological examination rate in our study resulted from the necessity of transvaginal ultrasound in addition to abdominal ultrasound in cases of suspected gynecological diseases in young women in order to reduce the incidence of negative appendectomy. Recently, although diagnostic value of laboratory parameters such as MPV, RDW and NAR has been evaluated in patients with suspected appendicitis, results of these studies are highly controversial (17). MPV is a measurement of thrombocyte size that is obtained as a part of routine complete blood count and is usually overlooked by clinicians. Changes in platelet counts can lead to changes in MPV. The size and activity of platelets can be influenced by cytokines such as interleukin IL-3 and IL-6. Elevated MPV levels have been reported in several diseases including chronic obstructive pulmonary disease (COPD), myocardial infarction, diabetes mellitus and high altitude (18). Increases in MPV levels are associated with chronic diseases, while decreases are related to acute diseases (19). In our study, the mean MPV value was not statistically significantly lower in both the PA group and NA group. Although there are a few studies about the role of MPV in acute appendicitis, the results of these studies are variable (18, 20). In a study comparing the healthy control group with patients having acute

appendicitis, MPV level was found to be significantly lower in the acute appendicitis group. In the same study, it was emphasized that MPV level should not be overlooked in suspected acute appendicitis cases (18). In another study, a significant reduction was found in MPV level of patients with appendicitis (21). In a study by Uyanik et al., no statistical significance was observed in MPV levels of patients with acute appendicitis (20). In another study, higher MPV levels were found in patients with acute appendicitis compared to the control group (17). In a meta-analysis of five studies including 2101 patients with acute appendicitis, it was reported that MPV can be used as a biomarker for the diagnosis of positive appendicitis and is a rapid and inexpensive indicator (22). In our study, in the gender-based evaluation, MPV values were statistically significantly lowered only in male patients in the PA group. Based on our findings, we believe that MPV values under the lower normal range may be affected by gender and requires further evaluation to be used as a biomarker for positive acute appendicitis. Recent studies have investigated the relationship between hyperbilirubinemia and vermiform of inflammation, and some of these studies have reported that bilirubin can be used as a specific marker of appendiceal perforation (23). In our study, TBIL levels were significantly higher in the PA group compared to the NA group. However, in gender-based evaluation, TBIL levels were significantly higher in male patients both in PA and NA groups. In a study by Akbulut et al., a TBIL cut-off $\geq$ 0.67 is an independent factor predicting acute appendicitis (24). Therefore, our study supports the latest literature in line with our findings. In addition, although the high CRP value in acute appendicitis has been reported in various studies, (12) our outcome of high CRP values in the PA group supports the literature. Although there are several studies about the use of various laboratory markers in the diagnosis of acute appendicitis that were mentioned above, there is still no scientific evidence on the use of blood parameters in predicting acute appendicitis. At this point, it seems possible that NA ratios can be reduced by correlating more than one laboratory data. In imaging examination, one of the most important findings for the diagnosis of acute appendicitis is appendicitis diameter. In the present study, appendicitis diameter was statistically significantly higher in PA group than in NA group. Similarly, in a study by Katipoglu et al., the mean appendicitis diameter was significantly higher in the positive appendectomy cases (25). The main limitations of this study are its retrospective design and being conducted in a single center. However, the number of our patients is relatively higher than the other studies in the literature. In addition, unlike the other studies in the literature higher MPV (female group) and TBIL values in the positive appendectomy cases will bring a new projection to the literature.

Conclusion

According to the results of our study, CRP and TBIL values significantly differed between positive and negative appendectomy patients. Therefore, these values may be used as specific biomarkers in predicting positive acute appendicitis. We believe that these results will contribute to the literature and will be guiding for future studies. However, further studies are needed to determine the laboratory parameters that can be used as diagnostic biomarkers.

Authors contributions: GC: conceived and designed the study; BM, EG: developed the study protocol, collected the data, GC, KO: analyzed and interpreted the data; BK: supervised the study.

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