Comparison of Clinical Features Between Patients with Positive and Negative Appendectomy

Guner Cakmak (✉ mdgunercakmak@gmail.com)

Sakarya Universitesi Egitim ve Arastirma Hastanesi

Kayhan Ozdemir

Sakarya Universitesi Egitim ve Arastirma Hastanesi

Research

Keywords: acute appendicitis, mean platelet volume, total bilirubin, negative appendectomy

Posted Date: July 30th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-46787/v1>

License: This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Version of Record: A version of this preprint was published at Van Medical Journal on January 1st, 2021.
See the published version at <https://doi.org/10.5505/vtd.2021.42402>.

Abstract

Objective: 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 (PA) (n:425) and negative appendectomy (NA) (n:425) and the data obtained were compared between these two groups.

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.

Results: The mean MPV value was found as 7.66 in PA groups and 7.90 in NA group, and the mean MPV value was statistically significantly lower in PA group, compared to NA groups ($p=0.034$). The mean TBIL value was 0.75 in PA group and 0.90 in NA group, and the mean TBIL value was statistically significantly lower in PA group ($p=0.034$). There was no statistically significant difference between the two groups in terms of the other studied laboratory parameters (for all $p>0.05$).

Conclusion: The mean MPV and TBIL values can 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.

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 (4). 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 (5).

Today, the incidence of appendicitis is increasing in developing countries (6). 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 known as "negative appendectomy" (NA) (7).

Complications of acute appendicitis include perforation, peritonitis and sepsis (8). This can increase the rate of negative appendectomy operations. Negative appendectomy rate (NLR) is defined as the incidence of removing appendices that are pathologically normal (9). Negative appendectomy leads to

prolonged hospitalization, morbidity and increased costs. 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 (10). However, owing to better imaging modalities, a constant decrease is seen in the rate of NAs (11). Gynecological pathologies in female patients in child bearing period mimic acute appendicitis, which can cause an increase in the rate of negative NAs (12).

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 (13). 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 & Methods

Data of a total of 2368 patients who were referred to our general surgery clinic with the presumed diagnosis of appendicitis and underwent appendectomy between and were retrospectively evaluated. Among these patients, 1518 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 850 patients were obtained and evaluated. Patients aged between 1–90 years. Patients were divided into two groups as positive (PA) (n:425) and negative appendectomy (NA) (n:425) and the data obtained were compared between these two groups.

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..... years. 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. Appendectomy operations 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.

Ethics Considerations

Before the beginning of the study, necessary ethics approval was received from the local ethics committee of our hospital. Since the study had a retrospective design, receiving informed consent from the patients was waived. 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 $\pm$ standard deviation, while categorical variables were given as frequency and percentage. $p < 0.05$ values were considered statistically significant.

Results

A total Of 850 patients were included in the study with 425 (50%) being in PA group and 425 (50%) in NA group. Of all patients included in the study, 480 (56.5%) were male and 370 (43.5%) were female. A total of 249 (58.6%) patients were male and 176 (41.4%) were female in PA group. Whereas, 231 (50.1%) were male and 212 (49.9%) were female in the NA group. No statistically significant difference was seen between both groups in terms of gender ($p > 0.05$).

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 ($p > 0.05$).

Appendectomy operations were performed with laparoscopic method in 199 (46.8%) of the patients in PA group and in 207 (48.7%) of the patients in NA group. The remaining patients underwent open surgery.

When status of having gynecological examination was examined among the female patients; 136 (77.3%) female patients in PA group and 177 (83.5%) female patients in NA group underwent gynecological examination.

Laboratory outcomes were examined and compared between the two groups. Accordingly, the mean WBC value was found as 9.77 in PA group and 9.70 in NA group, and there was no statistically significant difference between both groups ($p = 0.756$). The mean MPV value was found as 7.66 in PA groups and 7.90 in NA group, and the mean MPV value was statistically significantly lower in PA group, compared to NA groups ($p = 0.034$). NEU (%) value was found as 73.95 in PA group and 74.74 in NA group. No statistically significant difference was observed between the two groups in terms of the mean NEU (%) value ($p = 0.388$). The mean neutrophil count was found as 7.04 in the PA group and 7.29 in NA group, and no statistically significant difference was found between the two groups ($p = 0.269$). The mean CRP value was found as 58.86 in PA group and 49.62 in NA group. There was no statistically significant difference between both groups in terms of the mean CRP value ($p = 0.097$). When total bilirubin values were examined; the mean TBIL value was 0.75 in PA group and 0.90 in NA group, and the mean TBIL value was statistically significantly lower in PA group ($p = 0.034$).

In our study, the examined laboratory parameters were also compared between genders. Accordingly, the mean MPV value was statistically significantly lower in male patients compared to female patients in PA group ($p = 0.013$). NEU (%) value was statistically significant between genders both in PA and NA groups. Accordingly NEU (%) value was statistically significantly lower in male patients compared to female patients in both PA and NA groups ($p = 0.005$, $p < 0.001$; respectively). Neutrophil count was statistically significantly lower in male patients in NA group ($p = 0.036$). Finally, TBIL value was statistically significantly lower in female patients compared to male patients in NA group ($p = 0.022$).

When diameters of appendicitis were evaluated; the mean appendicitis diameter was found as 1.33 cm in PA group and 1.12 cm in NA group, and the mean appendicitis diameter was statistically significantly higher in PA group compared to NA group ($p < 0.001$) (Table 1).

Table 1
WBC, MPV, NEU (%), NEU, CRP and TBIL Parameters According to PA and NA groups

	PA (n = 425)	NA (n = 425)	p value
WBC	9.77 (22.60–2.68)	9.70 (25.50–0.95)	0.756"
MPV	7.66 (12.80–4.92)	7.90 (17.70–5.15)	0.034*
NEU (%)	73.95 (95.90–24.30)	74.74 (98.90 – 0.77)	0.388"
NEU	7.04 (39.40–1.07)	7.29 (46.60 – 0.10)	0.269"
CRP	58.86 (383 – 0.10)	49.62 (297 – 0.10)	0.097"
TBIL	0.75 (2.55 – 0.20)	0.90 (9.82 – 0.18)	0.034*

The comparison of MPV and TBIL values that were significant between PA and NA groups is seen in Fig. 1.

Discussion

Surgical excision 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 (14). As in our country, high rates of appendicitis cases have been reported in some other countries (15). Therefore, more effort should be made in order to reduce the incidence of NAR and its complications on patients and hospitals (16). 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 (17).

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 (16). 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 NLR has been evaluated in patients with suspected appendicitis, results of these studies are highly controversial (18).

MPV is a measurement of thrombocyte size that is obtained as a part of routine complete blood count, and is usually overlooked by clinicians (19). 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 (20). Increases in MPV levels are associated with chronic diseases, while decreases are related to acute diseases (21). In our study, the mean MPV value was statistically significantly lower in the PA group compared to NA groups ($p = 0.034$). Although there are a few studies about the role of MPV in acute appendicitis, the results of these studies are variable (20, 22). 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 (20). In another study, a significant reduction was found in MPV level of patients with appendicitis (23). In

a study by Uyanik et al., no statistical significance was observed in MPV levels of patients with acute appendicitis (22). In another study, higher MPV levels were found in patients with acute appendicitis compared to the control group (18). 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 (24). Our lower MPV levels in PA groups can be explained by the sequestration of larger platelets in the vascular segments of inflamed intestines. Based on our findings, we believe that MPV values under the lower normal range can be used as a biomarker for positive acute appendicitis cases.

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 (25, 26). In our study, TBIL levels were significantly lower in PA group compared to NA group ($p = 0.034$). However, TBIL levels were within the normal range in both groups. In a study by Akbulut et al., a TBIL cut-off ≥ 0.67 is an independent factor predicting acute appendicitis (27). However, we could not find any study in the literature investigating the relationship between TBIL and acute appendicitis. Therefore, we could not exactly compare our TBIL finding with the previous studies.

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.

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 ($p < 0.001$). Similarly, in a study by Katipoglu et al., the mean appendicitis diameter was significantly higher in the positive appendectomy cases (28).

Study Limitations

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 lower MPB and TBIL values in the positive appendectomy cases bring a new projection to the literature. Unlike the other studies, WBC and CRP values were not significant between PA and NA groups.

Conclusion

According to the results of our study, the mean MPV and TBIL values can 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.

Declarations

Ethical Approval and Consent to Participate: N/A

Consent for Publication: Informed consent form was obtained from the patient for this case report.

Availability of data and materials: N/A

Competing Interests: The authors declare no competing interests to disclose.

Funding: This case report did not receive financial support.

Acknowledgements: N/A

Conflict of Interest: The authors declare no conflict of interest regarding this study

Funding: This study did not receive financial support

Ethics Considerations: Informed consent form was obtained from the patients for this study to use patient information for publication purpose.

Authors' Information:

Guner Cakmak: Sakarya Training & Research Hospital, Department of General Surgery, Sakarya, Turkey

E mail: mdgunercakmak@gmail.com

ORCID: 0000-0003-4040-4635

Kayhan Ozdemir: Sakarya Training & Research Hospital, Department of General Surgery, Sakarya, Turkey

E mail: drkayhan1@gmail.com

ORCID: 0000-0003-4040-4635

Correspondence: Guner Cakmak

Sakarya Training & Research Hospital, Department of General Surgery, Sakarya, Turkey

E mail: mdgunercakmak@gmail.com

Adress: Sirinevler, Adnan Menderes Cad. Saglık Sok No:195, 54100 Adapazarı/Sakarya

Phone: +90 444 5 400

References

1. Tai HH, Ying CH, Chi W. Acute appendicitis or not: Facts and suggestions to reduce valueless surgery. *J Acute Med.* 2013;3(4):142–7.
2. Ferris M, Quan S, Kaplan BS, Molodecky N, Ball CG, Chernoff GW, et al. The global incidence of appendicitis: A systematic review of population-based studies. *Ann Surg.* 2017;266(2):237–41.
3. Tsai MC, Kao LT, Lin HC, Chung SD, Lee CZ. Acute Appendicitis Is Associated with Peptic Ulcers: A Population based Study. *Scientific Reports* 2015;5.
4. World Health Organization. Surgical care at the district hospital. World Health Organization, 2003.
5. Poletti PA, Becker M, Becker CD, et al. Emergency assessment of patients with acute abdominal pain using low-dose CT with iterative reconstruction: A comparative study. *Eur Radiol.* 2017;27(8):3300–9.
6. Sartelli M, Baiocchi GL, Di Saverio S, Ferrara F, Labricciosa FM, Ansaloni L, Coccolini F, Vijayan D, Abbas A, Abongwa HK, Agboola J. Prospective observational study on acute appendicitis worldwide (POSAW). *World Journal of Emergency Surgery.* 2018 Dec;13(1):19.
7. Ruffolo C, Fiorot A, Pagura G, Antoniutti M, Massani M, Caratozzolo E, et al. Acute appendicitis: What is the gold standard of treatment? *World J Gastroenterol.* 2013;19(47):8799–807.
8. Webb EM, Nguyen A, Wang ZJ, Stengel JW, Westphalen AC, Coakley FV. The negative appendectomy rate: Who benefits from preoperative CT? *AJR Am J Roentgenol.* 2011;197(4):861–6.
9. Raja AS, Wright C, Sodickson AD, Zane RD, Schiff GD, Hanson R, et al. Negative appendectomy rate in the era of CT: An 18-year perspective. *Radiology.* 2010;256(2):460–5.
10. Cuschieri J, Florence M, Flum DR, Jurkovich GJ, Lin P, Steele SR, et al. Negative appendectomy and imaging accuracy in the Washington State Surgical Care and Outcomes Assessment Program. *Ann Surg.* 2008;248(4):557–63.
11. Seetahal SA, Bolorunduro OB, Sookdeo TC, Oyetunji TA, Greene WR, Frederick W, Cornwell EE, Chang DC, Siram SM. Negative appendectomy: a 10-year review of a nationally representative sample. *The American Journal of Surgery.* 2011 Apr 1; 201(4): 433–437.
12. Hatipoglu S, Hatipoglu F, Abdullayev R. Acute right lower abdominal pain in women of reproductive age: Clinical clues. *World J Gastroenterol.* 2014;14:4043–9.
13. Yu CW, Juan LI, Wu MH, Shen CJ, Wu JY, Lee CC. Systematic review and meta-analysis of the diagnostic accuracy of procalcitonin, C-reactive protein and white blood cell count for suspected acute appendicitis. *Br J Surg.* 2013 Feb;1(3):322–9. 100).
14. <https://dx.doi.org/10.1186/1471-2482-6-15>
Sack U, Biereder B, Elouahidi T, Bauer K, Keller T, Tröbs RB. Diagnostic value of blood inflammatory markers for detection of acute appendicitis in children. *BMC Surgery.* 2006;6(1):15–15. Available from: <https://dx.doi.org/10.1186/1471-2482-6-15>.
15. Kirkil C, Karabulut K, Aygen E, Ilhan YS, Yur M, Binnetoğlu K, et al. Appendicitis scores may be useful in reducing the costs of treatment for right lower quadrant pain. *Ulus Travma Acil Cerrahi Derg.* 2013;19:13–9.

16. Joshi MK, Joshi R, Alam SE, Agarwal S, Kumar S. Negative Appendectomy: an Audit of Resident-Performed Surgery. How Can Its Incidence Be Minimized? *Indian Journal of Surgery*. 2015 Dec;1(3):913–7. 77).
17. Wagner PL, Eachempati SR, Soe K, Pieracci FM, Shou J, Barie PS. Defining the current negative appendectomy rate: for whom is preoperative computed tomography making an impact? *Surgery*. 2008;144:276–82.
18. Narci H, Turk E, Karagulle E, Togan T, Karabulut K. The role of red cell distribution width in the diagnosis of acute appendicitis: a retrospective case-controlled study. *World J Emerg Surg*. 2013;8:46.
19. Beyazit Y, Sayilir A, Torun S, Suvak B, Yesil Y, Purnak T, et al. Mean platelet volume as an indicator of disease severity in patients with acute pancreatitis. *Clin Res Hepatol Gastroenterol* 2012;36;162-8.
20. AlbayrakY, Albayrak A, Albayrak F, Yildirim R, Aylu B, Uyanik A, et al. Mean Platelet Volume: A New Predictor in Confirming Acute Appendicitis Diagnosis. *Clin Applied Thrombosis/Hemostasis*. 2011;17:362–6.
21. Erdem H, Aktimur R, Cetinkunar S, Reyhan E, Gokler C, Irkorucu O, Sozen S. Evaluation of mean platelet volume as a diagnostic biomarker in acute appendicitis. *International Journal of Clinical Experimental Medicine*. 2015;8(1):1291–5.
22. Uyanik B, Kavalci C, Arslan ED, Yilmaz F, Aslan O, Dede S, et al. Role of Mean Platelet Volume in Diagnosis of Childhood Acute Appendicitis. *Emerg Med Int*. 2012;2012:823095.
23. Bilici S, Sekmenli T, Göksu M, Melek M, Avci V. Mean Platelet volume in diagnosis of acute appendicitis in children. *Afr Health Sci*. 2011;11:427–32.
24. Fan Z, Zhang Y, Pan J, Wang S. Acute Appendicitis and Mean Platelet Volume: A Systemic Review and Meta-analysis. *Ann Clin Lab Sci*. 2017;47(6):768–72.
25. D’Souza N, Karim D, Sunthareswaran R. Bilirubin: a diagnostic marker for appendicitis. *Int J Surg*. 2013;11:1114–7.
26. Muller S, Falch C, Axt S, et al. Diagnostic accuracy of hyperbilirubinaemia in anticipating appendicitis and its severity. *Emerg Med J*. 2014;0:1–5.
27. Akbulut S, Koc C, Sahin TT, et al. Akut Apandisit ve Perfore Apandisiti öngören faktörlerin belirlenmesi. *Ulus Travma Acil Cerrahi Derg*. Ahead of Print: UTD-60344. doi: 10.14744/tjtes.2020.60344.
28. Katipoglu B, Aygun A, Cinar H. The effect of appendix diameter on perforation in acute appendicitis cases. *CMJ*. 2019;41(2):392–7.

Figures

Figure 1

Comparison of MPV and TBIL values between PA and NA groups.