

Can Appendiceal Neoplasms Be Predicted in Patients with Presumed Acute Appendicitis?

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ABSTRACT

Objective: The detection of malignancy in the final pathology report of patients undergoing surgery for acute appendicitis is a nasty surprise for both the patient and the clinician. To improve the management of this situation, we analyzed clues for predicting possible neoplasms.**Methods:** We analyzed in detail the data of patients operated on in our department with a preliminary diagnosis of acute appendicitis over 42 months. The group whose final pathology was reported as primary appendiceal neoplasm was compared with the acute appendicitis group.**Results:** Appendiceal neoplasm was detected in 16 patients (1%). Half of these were mucinous epithelial neoplasms. Neuroendocrine tumors (18.7%) were the second most common neoplasm. According to the logistic regression model, low hemoglobin level ($p<0.01$) and low Alvarado score ($p:0.02$) were the two most valuable factors in the prediction of primary appendiceal neoplasms. Laboratory findings of high neutrophil/lymphocyte ratio ($p<0.01$) and plastron formation on imaging ($p:0.03$) were more common in the neoplasm group. Advanced age, comorbidity, immunosuppression and inflammatory bowel diseases (IBD) were other characteristics of the neoplasm group.**Conclusions:** Appendiceal neoplasms should always be considered in anemic patients with relatively low Alvarado scores.**Keywords:** Appendicitis, Appendectomy, Appendiceal Neoplasms, Appendiceal Tumor

INTRODUCTION

Primary appendiceal neoplasms are a rare condition that is usually encountered incidentally in around 1% of appendectomies performed for acute appendicitis, and this rate may be as high as 1.7% in some studies from the United States [1,2]. The lifetime incidence of acute appendicitis is around 8%, which increases the importance of incidental appendiceal neoplasms [3].

Although it is known that symptomatic appendiceal cancer cases present with signs of acute appendicitis, patients presenting with nonspecific findings constitute the group with a more advanced

stage and worse prognosis [4]. Appendiceal neoplasms may have a wide histological diversity and highly variable biological behavior. The most common neoplasms are mucinous epithelial lesions, followed by neuroendocrine tumors and non-mucinous epithelial neoplasms [5]. As in the stomach and colon, signet ring cell carcinoma has a more aggressive biological behavior and fortunately represents a smaller group. Goblet cell carcinoma is known to be more aggressive than malignant carcinoid but has a better prognosis than colonic-type cancers. Lymphoma, sarcoma and nerve sheath tumors constitute a very rare non-epithelial group [6].

It may be useful to consider some parameters when planning interval appendectomy in cases of plastron appendicitis, which is especially common in elderly patients, to prevent the progression of possible neoplasms [7]. At the same time, inadequate patient information about the results of histologic examination after appendectomy may bring some legal problems. Therefore, we aimed to present this retrospective study to improve the approach to patients with suspected neoplastic lesions before appendectomy and to increase awareness of this issue.

MATERIALS AND METHODS

The study was conducted on the data of patients operated with a preliminary diagnosis of acute appendicitis in Şehit Prof. Dr. İlhan Varank Sancaktepe Training and Research Hospital. Patients signed an informed consent form regarding the use of medical records and ethics committee approval was obtained from the same center. Biological and demographic information, imaging and laboratory results were collected from the hospital information management system and operative findings were analyzed from patient files. Patients receiving systemic chemotherapy for malignancy, pregnant patients and the population younger than 18 years were excluded. Patients who underwent surgery for a different cause of acute abdomen but were found to have appendicitis as the primary focus were also excluded. The study included 1598 patients who underwent surgery in the 42 months between September 2019 and February 2023.

Duration of symptoms, American Society of Anesthesiologists score (ASA), immunosuppression status and Alvarado scores

were also questioned. Patients with primary appendiceal neoplasia (neoplasm group) and patients with appendicitis (appendicitis group) were compared in terms of independent variables. The neoplasm group was divided into epithelial tumors and neuroendocrine tumors. Epithelial lesions were classified as mucinous and non-mucinous.

Statistical Analysis

Data distribution was tested by Shapiro-Wilk analysis. Pearson chi-square test was used for categorical variables and the Mann-Whitney U test for continuous variables. The logistic regression method was used for predictive value analysis. Cut-off values were calculated by the receiver operating characteristic curve (ROC). $P \leq 0.05$ was considered statistically significant. All analyses were performed with SPSS version 22 for Windows software.

RESULTS

The median age of the 1598 patients included in the study was 25 years (18-82). According to Tabachnick, nonparametric tests were used for age and other data that did not show normal distribution and are emphasized with * in the tables [8]. Of the total patients, 646 were female (40.4%). There was a total of 11 patients with severe life-threatening conditions such as sepsis, newly diagnosed myocardial infarction or other serious life-threatening conditions (ASA 4). The mean body mass index was 26.8. Symptom duration at presentation ranged from 12 to 72 hours. Severe heart failure, uncontrolled diabetes, chronic renal failure, chronic lung parenchymal disease or neurologic problems were considered as comorbidities. The number of patients receiving treatment for inflammatory bowel disease was 9 (0.56%) and the number of patients receiving high-dose steroids and other immunosuppressants for different reasons was 26 (1.6%). Biological data are summarized in Table 1 and laboratory and imaging findings are summarized in Table 2.

The appendiceal neoplasm was detected in only 16 patients, and its rate among all appendectomies is around 1%. Mucinous type adenoma or adenocarcinoma was detected in 8 of them (50%). The neuroendocrine tumor was observed in three patients (18.7%), colonic type adenocarcinoma was observed in two patients (12.5%), and signet ring cell carcinoma, goblet cell carcinoma and lymphoma were detected in one patient each (6.2%). Patients with appendiceal neoplasm were relatively older ($p < 0.01$). In parallel, higher ASA scores and body mass indexes in the neoplasm group and more comorbidities in this

Main Points:

- In patients with a prediagnosis of acute appendicitis, the rate of neoplasm detection in the final pathology is approximately 1%.
- The fact that it is the most common acute abdomen surgery performed worldwide increases the importance of this rate.
- Since preoperative prediction of this condition may change both the operative strategy and the treatment plan, a number of parameters were analysed.
- Appendiceal neoplasm should be considered and managed accordingly, especially in anaemic patients with low Alvarado score

group were thought to be associated with advanced age. It was statistically significant that inflammatory bowel diseases and immunosuppressed patients were more common in the neoplasm group (p:0.003, p:0.02, respectively). Weak immunity, especially in association with intestinal inflammation, was thought to be a facilitator for appendiceal neoplasms. Gender seemed to be insignificant in terms of appendiceal neoplasms. Smoking habits and the duration of appendicitis-specific symptoms did not provide any clue for appendiceal neoplasms. A lower Alvarado score (6.5-7.1) was statistically significant for tumor patients. The most striking imaging finding was that plastron formation was more common in the neoplasm group (p:0.03). Although the mean appendix diameter (mm) was higher, it was below the statistical significance level (12.6-11.8). When the laboratory findings were analyzed, higher neutrophil count versus lower lymphocyte count suggested that the neutrophil/lymphocyte ratio could give an idea about appendiceal neoplasms.

Table 1. Demographic and biological characteristics between the two groups

Biological features	Neoplasm	Appendicitis	P value
Age*	45	25	<0.01
Sex Male	11(68.8%)	941(59.5%)	0.45
BMI	26.9	25.2	0.05
ASA score	2(1-4)	2(1-4)	0.02
Smoker	6(37.5%)	398(25.2%)	0.19
Comorbidity	8(50%)	178(11.3%)	<0.01
IBD	2(12.5%)	7(0.4%)	0.003
Immunosuppression	2(12.5%)	24(1.5%)	0.02
Alvarado score	6.5	7.1	0.04
DoS*	20.5	22.4	0.13

Chi-Square , Student’s t-test, *Mann Whitney-U

BMI: body mass index; ASA: American Society of Anesthesiologists; IBD: inflammatory bowel disease; Dos: duration of symptoms

Table 2. Radiologic and laboratory differences between the two groups

Imaging & Laboratory	Neoplasm	Appendicitis	P value
DoA(mm)	12.6	11.8	0.17
Appendicolith	4(25%)	466(29.5%)	0.79
Plastron	2(12.5%)	28(1.8%)	0.03

Abscess	1(6.3%)	79(5%)	0.56
Phlegmon	2(12.5%)	94(5.9%)	0.24
IAF	3(18.8%)	206(13%)	0.35
WBC($\times 10^9/L$)	14.2	13.1	0.04
Lymphocyte($\times 10^9/L$)	1.6	1.9	0.01
Neutrophil($\times 10^9/L$)	12	11.2	0.1
Hemoglobin(g/dL)	12.2	13.9	<0.01
Platelet* ($\times 1000/\mu L$)	248.8	303.8	0.05
NLR	7.7	6.2	<0.01
PLR*	160	155.8	0.43

Chi-Square , Student’s t-test, *Mann Whitney-U

DoA: diameter of appendix; IAF: intra abdominal fluid; WBC: white blood cell; NLR: neutrophil/lymphocyte ratio; PLR: platelet/lymphocyte ratio

When the independent variables that differed between the neoplasm group and the appendicitis group were examined by logistic regression analysis, it was seen that a low hemogram value was the most reliable indicator in predicting neoplasm (p<0.01). It was determined that each 1-point decrease in the Alvarado score increased the probability of neoplasm by 0.4 times (p:0.02) (Table 3). Roc curves for both parameters were shown in Figure 1 (area under the curve for hemoglobin 0.83, for Alvarado score 0.65). The cut-off value for hemoglobin was 13.45 g/dL and for Alvarado score was 6.5.

Table 3. Impact of variables on prediction of appendiceal neoplasms

Variables	Exp(B)	95% C.I. for EXP(B)		P value
		Lower	Upper	
Age	1.040	0.981	1.103	0.19
BMI	1.072	0.908	1.266	0.41
ASA score	1.392	0.503	3.853	0.52
Comorbidity	0.484	0.104	2.247	0.35
IBD	0.246	0.011	5.495	0.37
Immunosuppression	0.540	0.015	19.603	0.73
Alvarado score	0.415	0.190	.906	0.02
Plastron	0.188	0.010	3.541	0.26
WBC	2.371	0.587	9.574	0.22
Lymphocyte	0.949	0.033	26.968	0.97
Neutrophil	0.502	0.088	2.869	0.43

Hemoglobin	0.530	0.376	.746	0.00
Platelet	0.999	0.995	1.003	0.54
NLR	1.260	0.409	3.878	0.68

Logistic regression analysis(enter method)

BMI: body mass index; ASA: American Society of Anesthesiologists; IBD: inflammatory bowel disease; WBC: white blood cell; NLR: neutrophil/lymphocyte ratio

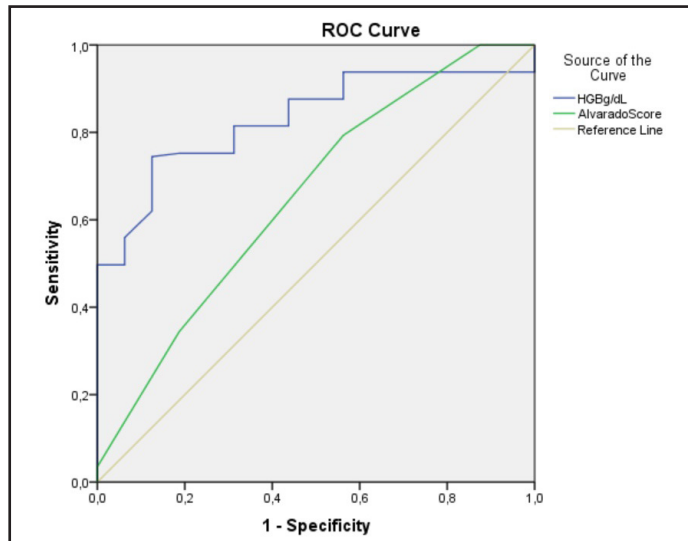


Figure 1. ROC analysis of two important parameters in the prediction of appendiceal neoplasms.

DISCUSSION

Since appendectomy is one of the most frequently performed emergency operations both in our country and worldwide, we believe that it deserves a special approach in terms of follow-up and outcomes [9]. If some predictive factors for appendiceal neoplasms can be determined preoperatively, the surgical technique and follow-up strategy can be appropriately developed. For resection to be performed by oncological principles, preparations such as preparation of erythrocyte suspension in the preoperative period, informing the patient, obtaining appropriate surgical consent and preparing the necessary surgical materials are required. In this way, the need for repeat surgery can be eliminated. Even if an appendiceal neoplasm is not detected intraoperatively, the presence of possible risk factors will keep in mind that the case may not be a simple appendicitis, so that close follow-up of the final pathology report may prevent advanced disease [10].

When patients who were operated on for more than 4 years

were carefully analyzed, it was observed that the group in which appendiceal neoplasms were detected consisted of significantly older patients, which is in line with the literature [11, 12]. Increasing body mass index and the high incidence of comorbidities can be considered as a result of advanced patient age, although they are not directly related to the neoplasm.

Although female gender has been considered a risk factor for appendix malignancy in some studies [13], the general opinion in the literature is that gender is not a determinant [14]. In our study, gender was not a significant variable. The significantly lower Alvarado score in the neoplasm group ($p:0.04$) may be because pain migration is a symptom specific to acute appendicitis. Studies are emphasizing this situation [12]. Inflammatory bowel diseases ($p:0.003$) and immunosuppression ($p:0.02$) were found to be two different parameters that were more common in the appendiceal neoplasm group. In the literature, there are articles stating that the association of inflammatory bowel diseases and appendiceal carcinoids has no special significance [15], and there are also authors claiming that this is not a simple coincidence [16]. Although the increased risk of colon adenocarcinoma due to long-term epithelial inflammation has been emphasized, no consensus has been reached for isolated tumors of the appendix [17, 18]. Based on the data from our study, we suggest that weak immunity may constitute a risk for appendiceal neoplasms and that colonic inflammation further increases this risk.

When preoperative imaging features and perioperative findings were considered, it was found that only plastron formation was significantly higher in appendiceal neoplasms (12.5% - 5.9% $p:0.02$). It was found that this condition was described as a suspicious mass in some publications in the literature, while focal dilatation of the appendix was emphasized in others [12, 19]. In laboratory results, the mean total white blood cell count (WBC) was slightly higher in neoplasm patients, while lymphocytosis was more prominent in patients with acute appendicitis ($p:0.01$). Considering the publications that consider relatively low WBC as an independent predictor of appendiceal tumor [20], low hemoglobin value and high NLR ratio were considered to be more valuable parameters ($p<0.001$).

Limitations

The only limitation of the study was the lack of a standardized description of the plastron formation during perioperative evaluation, which was compensated by careful CT examination and comparison.

CONCLUSION

As a result of both the biological characteristics of the patients and laboratory findings, hemoglobin value was found to be the most valuable finding as a neoplasm predictor. It should be kept in mind that the operation of anemic patients with relatively low Alvarado scores under more optimal conditions will make undeniable contributions to improving the prognosis of the disease.

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