



## EVALUATION OF NEUROENDOCRINE TUMOR FREQUENCY AND PREDICTIVE VALUE OF NEUTROPHIL-LYMPHOCYTE RATIO IN ACUTE APPENDICITIS CASES

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### ARTICLE INFO

### ABSTRACT

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**Objective:** The aim of this study was to investigate the efficacy of simple accessible laboratory parameters such as neutrophil-lymphocyte ratio (NLR) in the diagnosis of acute appendicitis and the incidence of neuroendocrine tumors in patients operated with an initial diagnosis of acute appendicitis.

**Materials and methods:** Postoperative pathology diagnosis, neutrophil-lymphocyte ratio, age, sex, perforation of 952 patients with an initial diagnosis of acute appendicitis between January 2009 and December 2015 were reviewed retrospectively. Acute appendicitis cases were divided into two groups as complicated (perforated) and simple uncomplicated cases. NLR ratio was calculated. Receiver operating characteristic (ROC) curve analysis was used to define important parameters in multivariate analysis. Cut-off values, sensitivity, specificity and accuracy calculations were made for the parameters under the curve area (AUC) > 0.600.

**Results:** 23 patients were excluded from the study due to incomplete data. Normal appendix in 1 (0.1%), endometriosis in 1 (0.1%), adenocarcinoma in 4 (0.4%) cases, neuroendocrine tumor in 7 (0.8%) cases, lymphoid hyperplasia in 138 (14.9%) cases and acute appendicitis was detected in 778 (83.7%) cases. Of the 778 patients, 124 (15.9%) had a perforation. NLR sensitivity and specificity were found in cases with acute appendicitis but not in complicated cases. However, the cut-off point of NLR with sensitivity of 85% and a specificity of 94% was found to be > 4,526 in the complicated acute appendicitis.

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**Conclusion:** NLR > 4,526 in subjects with perforation was found to be significantly associated with acute appendicitis.

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## INTRODUCTION

Appendicitis is one of the most common causes of acute abdominal pain. It is one of the most common indications for

abdominal surgery worldwide (1, 2). Appendicitis often occurs in the 2nd and 3rd decades. It is 1.4 times more common in males than in females [3]. Appendiceal

obstruction can be due to fecalite, lymphoid hyperplasia, infectious conditions and tumors (4, 5). Among the laboratory findings of patients with acute appendicitis, a mild leukocytosis is the most common (6). Approximately 80% of patients have left-sided gliding with neutrophil predominance with leukocytosis. In patients with acute appendicitis, the high WBC count has a sensitivity of 80% and a specificity of 55 (7-9). In addition, the mean number of WBCs increased in patients with gangrenous or perforated acute appendicitis compared to the other cases (10).

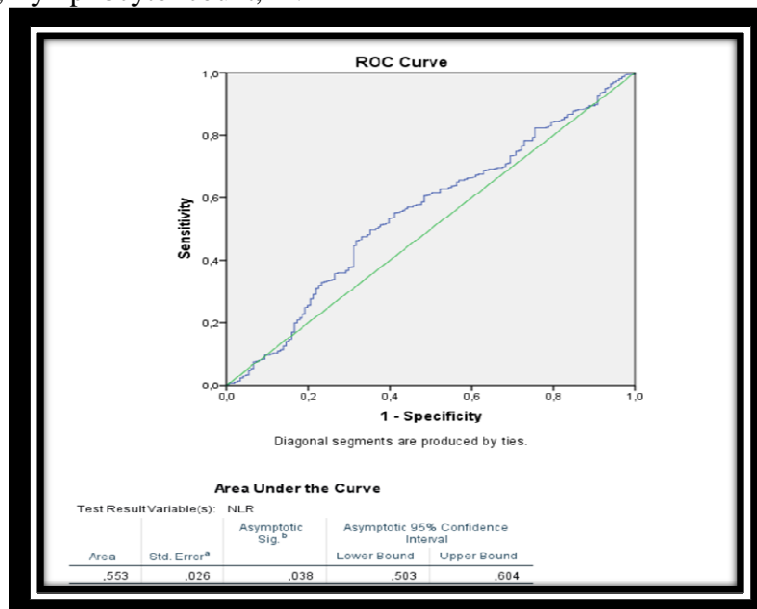
**MATERIAL AND METHODS:**

Postoperative pathology diagnosis, neutrophil-lymphocyte ratio, age, sex, and perforation were evaluated retrospectively in 952 patients with an initial diagnosis of acute appendicitis between January 2009 and December 2015. 23 cases were excluded from the study due to missing data. Patients with acute appendicitis with perforation were divided into two groups as uncomplicated, uncomplicated cases. Demographic data, preoperative WCC, neutrophil count, lymphocyte count, NLR

were calculated. Postoperative histopathological diagnoses were recorded. ROC curve analysis was used to define important parameters in multivariate analysis. Cut-off values, sensitivity, specificity and accuracy calculations were made for the parameters under the curve area (AUC)> 0.600.

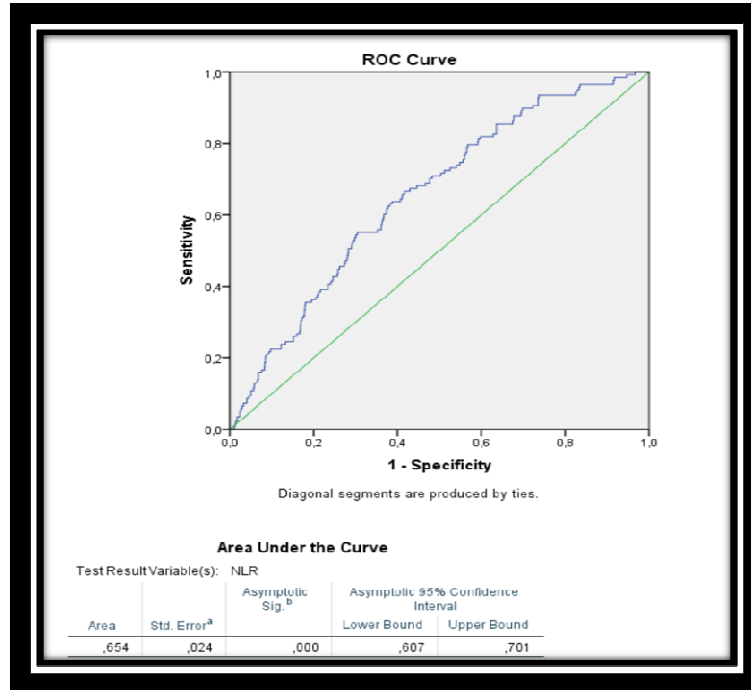
**RESULTS:**

The histopathological results of 929 patients were normal appendix in 1 (0.1%), endometriosis in 1 (0.1%), adenocarcinoma in 4 (0.4%), neuroendocrine tumor in 7 (0.8%), lymphoid hyperplasia in 138 (14.9%), 778 (83.7%) had acute appendicitis. The mean age of 778 patients with acute appendicitis was  $34.42 \pm 13.9$ . Of the patients, 316 (40.6%) were females while 462 (59.4%) were males. Of the 778 patients, 124 (15.9%) had a perforation. In the case of uncomplicated acute appendicitis cases, the area under the curve was 0.553. Also, since the sensitivity and specificity were low as the likelihood ratio <2, a certain cut off value was not considered for NLR (figure 1).



**Figure 1.** Roc curve analysis in patients with uncomplicated acute appendicitis. In the cases of complicated acute appendicitis, the area under the curve was 0.654. Since the likelihood ratio was > 2, the cutoff value was determined for NLR. The

cut-off value for NLR was found to be 4.526 complicated acute appendicitis cases. with 85% sensitivity and 94% specificity in



**Figure 2.** Roc curve analysis in patients with perforated acute appendicitis.

**Table 1.** Histopathological and demographic data in patients who were operated with the diagnosis of acute appendicitis.

Histopathological diagnosis	Gender n(%)		Perforation n(%)		Total
	Female	Male	Negative	Positive	
Appendicitis	316 (40.6 %)	462 (59.4%)	654 (84.1%)	124 (15.9%)	778
Lymphoid Hyperplasia	51 (37%)	87 (63.%)	125 (90.6%)	13 (9.4%)	138
Adenocarcinoma	3 (75%)	1 (25%)	4 (100%)	0 (0%)	4
Neuroendocrine tumor	2 (28.6%)	5 (71.4%)	6 (85.7%)	1 (14.3%)	7
Endometriosis	1 (100%)	0 (0%)	1 (100%)	0 (0%)	1
Normal	0 (0%)	1 (100%)	1 (100%)	0 (0%)	1
Total	373 (40.2%)	556 (59.8%)	791 (85.1%)	138 (14.9%)	929

**DISCUSSION**

Most of the patients who underwent abdominal surgery for acute abdomen still have acute appendicitis in the world in the etiology (1-2). In acute appendicitis cases, it may cause acute abdominal disease by

causing obstruction in benign or malign tumors except for infectious process. In our study, 4 (0.4%) cases had adenocarcinoma and 7 (0.8%) patients had neuroendocrine tumor appendicitis. In less than 3% of patients undergoing an appendectomy,

carcinoid tumor with primary appendix tumor, goblet cell carcinoma, lymphoma, mucocele, primary adenocarcinoma, and mucinous cyst are adenocarcinomas. A carcinoid tumor is the most common primary appendix tumor. They develop from enterochromaffin or Kulchitsky cells of the neuroendocrine system. The incidence of carcinoid tumor was 0.3-0.9%. It is more common in women (11-14). In our study, the mean age of cases with carcinoid tumor was  $30.14 \pm 9$ . Five (71%) of the patients were males while 2 (29%) were females. Appendix carcinoid tumors are often incidental with an appendectomy. It is very difficult to diagnose during surgery without histopathological examination. For the diagnosis of acute appendicitis, the experience of the examiner is the most important factor. In addition, ultrasound, computed tomography or MR imaging improve the sensitivity of the diagnosis (15-17). However, in some cases, the physician may not have the possibility of radiological imaging. The aim of this study is to evaluate the cheaper, more easily accessible NLR ratio. Kahramanca et al. (18) reported a high likelihood ratio of acute appendicitis in patients with a cut-off value of  $> 4.68$  in NLR. Goodman et al. (19) reported that in 298 patients with appendicitis,  $\text{NLR} > 3.5$  would increase the sensitivity in the diagnosis. Yazici et al. (20) reported a high likelihood ratio of acute appendicitis in patients with a cut-off value of  $\text{NLR} > 3.5$ . In our study, roc curve analysis for NLR was found to be low in uncomplicated acute appendicitis cases. In cases with complicated acute appendicitis, the cut-off value was determined by calculating the likelihood ratio for  $\text{NLR} > 2$ . The cut-off value for NLR was found to be 4.526 with 85% sensitivity and 94% specificity in complicated acute appendicitis cases. Ishizuka et al. (21) argued that gangrenous appendicitis is important in patients who

underwent appendectomy with a neutrophil-lymphocyte ratio  $> 8$ .

### CONCLUSION

Laboratory parameter  $\text{NLR} > 4.526$ ; since it is easily accessible, cost-effective, it has a reliable likelihood ratio in the diagnosis of complicated cases with acute appendicitis. More work is needed to use NLR in clinical practice.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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