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RESEARCH

DIAGNOSTIC VALUE OF NEUTROPHIL/LYMPHOCYTE RATIO IN GERIATRIC CASES WITH APPENDICITIS

ABSTRACT

Introduction: The aim of this study was to investigate the efficacy of the neutrophil/lymphocyte ratio in geriatric patients who consulted to the emergency department with a diagnosis of acute appendicitis.

Materials and Method: A total of 43 cases over 65 years of age operated with a diagnosis of appendicitis (Group 1) between January 2009 and December 2013, and 81 unoperated cases (Group 2; Control Group) were evaluated retrospectively. Age, gender, leukocyte count, neutrophil and lymphocyte values, neutrophil/lymphocyte ratio, imaging, and operative and pathological findings for both groups were evaluated.

Results: A significant difference was found between Groups 1 and 2 with respect to leukocyte and neutrophil counts and neutrophil/lymphocyte ratio ($p<0.001$). No statistically significant differences were found for distribution of age, lymphocyte count, and gender. Receiver operating characteristics curve was drawn with existing data for neutrophil/lymphocyte ratio; when we take 3,93 for cut-off value sensitivity was %92.5 and spesifity was %59.3. In pathological evaluation of 43 patients in Group 1, perforated (n=4), gangrenous and phlegmonous (n=36) and acute (n=3) appendicitis were detected.

Conclusion: Preoperatively, the estimated neutrophil/lymphocyte ratio can be accepted as easily available, adjunctive data that contributes to the diagnosis of appendicitis at a lower cost.

Key Words: Aged; Geriatric; Appendicitis; Neutrophils; Leukocytes.

ARAŞTIRMA

GERİATRİK YAŞ GRUBUNDA GÖRÜLEN AKUT APANDİSİT OLGULARINDA NÖTROFİL/LENFOSİT ORANININ TANISAL DEĞERİ

ÖZ

Giriş: Bu çalışmanın amacı, acil tıp kliniğine başvurup akut apandisit tanısı alan geriatrik yaş grubundaki olgularda nötrofil/lenfosit oranının tanısal değerini araştırmaktır.

Gereç ve Yöntem: Ocak 2009–Aralık 2013 yılları arasında, apandisit tanısıyla ameliyat edilmiş, 65 yaş üstü 43 olgunun (Grup 1) ve ameliyat edilmemiş, 81 olgunun (Grup 2, kontrol grubu) hasta dosyaları retrospektif olarak değerlendirildi. Olguların; yaş, cinsiyet, lökosit sayımı, nötrofil değeri, lenfosit değeri, nötrofil lenfosit oranı, görüntüleme bulguları, ameliyat bulguları ve patolojik incelemeleri değerlendirmeye alındı.

Bulgular: Grup 1 ve grup 2 arasında, lökosit sayısı, nötrofil sayısı ve nötrofil / lenfosit oranı açısından anlamlı oranda farklılık olduğu saptandı ($p<0.001$). Yaş, lenfosit sayısı ve cinsiyet dağılımı açısından istatistiki olarak anlamlı fark saptanmadı. Mevcut veriler ile nötrofil / lenfosit oranı için alıcı işletim karakteristiği eğrisi elde edildiğinde; eşik değeri 3.93 olarak alındığında sensitivite %92.5, spesifite %59.3 olarak saptandı. Patolojik değerlendirmede (Grup 1); 4 olguda perfore apandisit, 36 olguda gangrene, flegmone apandisit ve 3 olguda akut apandisit saptandı.

Sonuç: Ameliyat öncesi bakılan nötrofil/lenfosit oranının; apandisit tanısı için, düşük maliyetle ve kolayca elde edilebilecek, değerli bir veri olduğu görülmüştür.

Anahtar Sözcükler: Geriatri; Apandisit; Nötrofil; Lökosit.

Introduction

Acute appendicitis (AA) is the most frequently seen cause of acute abdomen. Its incidence is 7% in all age groups, while the incidence of perforation in patients with a diagnosis of AA ranges from17-20%. Although the mortality rate in the general population is below 1%, with aging (>60 years) its incidence approaches 50% (1-3). Most frequently seen symptoms and signs include leukocytosis and lower abdominal quadrant tenderness.

Despite imaging modalities and highly sensitive laboratory tests introduced into clinical use with developing technology, diagnostic difficulties are still experienced and higher perforation rates are encountered. However, in many published series, higher perforation (15-45%) and negative appendectomy (7-25%) rates demonstrate that despite evolving technological opportunities and clinical experience, a perfect diagnostic method has not yet been developed (4).

In recent years, some researchers have reported on the predictive value of the neutrophil/lymphocyte ratio (NLR) for inflammation, which can be used as a diagnostic parameter in the perioperative diagnosis of AA (5,6,7). Because of the favourable cost-effectiveness of this test, we aimed to investigate the efficacy of NLR in geriatric patients who consulted to the emergency department with a diagnosis of AA.

Materials and Methods

This study was approved by Bagcilar Training and Research Hospital, Clinical Ethics Committees (2014/246, 03.06.2014). The medical files of 43 cases aged over 65 (total N=5000) operated with the diagnosis of AA (Group 1) in the Clinics of General Surgery at our tertiary center between January 2009 and December 2013, and 81 unoperated cases (Group 2; Control Group) who were consulted to the emergency department with complaints of abdominal pain, were evaluated retrospectively.

Age, sex, leukocyte count, neutrophil and lymphocyte values, neutrophil/lymphocyte ratio, imaging, and operative and pathological findings were evaluated. Measurements of leukocyte, neutrophil and lymphocyte values were performed using an automated cell counter. Normal values for leukocyte counts were accepted as 4500-10300/mm^3.

Histopathological examination results were grouped as perforated appendicitis and gangrenous-phlegmenous appendicitis. Patients in Group 1 were operated and after completion of their observation period in the service, they were discharged as cured. Patients evaluated in Group 2 as having no remarkable characteristic findings were discharged from the intensive care unit after regression of clinical findings with medical treatment.

Statistical Analyses

Data were analyzed using the Statistical Package for the Social Sciences 17.0 for Windows (SPSS Inc., Chicago, IL). For categorical data (age, leukocyte value, neutrophil value, lymphocyte value, NLR), Student's t-test was used. Comparison of gender groups was performed using the $^{-2}$ test. In Group 1, NLR subgroups analyses done with Mann Whitney U test. Receiver operating characteristics (ROC) curve was drawn with existing data for NLR. All differences associated with a chance probability of .05 or less were considered statistically significant.

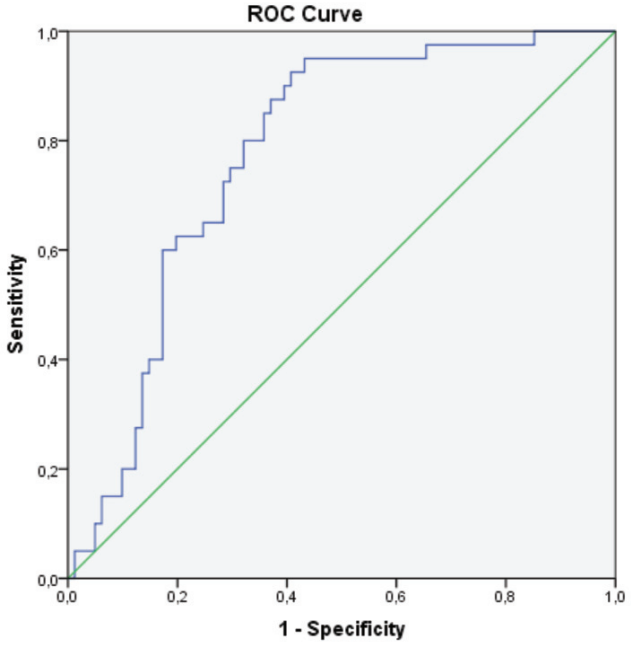
Results

The following parameters were evaluated; mean age, Group 1=73.69±6.99 years and Group 2=75.3±6.48 years; male/female ratio, Group 1=27/16 and Group 2=46/35; leukocyte count, Group 1=13.63±3.46 and Group 2=8.73±3.34 10^3/mm^3; neutrophil count, Group 1, 11.11±3.26 10^3/mm^3 and Group 2, 6.24±3.43 10^3/mm^3; lymphocyte count, 1.49±0.95 10^3/mm^3 and Group 2, 1.71±0.75 10^3/mm^3; NLR, Group 1, 10.15±6.7 and Group 2, 5.78±6.99 (Table 1).

Table 1— Demographic and Hematological Data (Leukocyte, Neutrophil and Lymphocyte Counts) and Neutrophil/Lymphocyte Ratio in Groups 1 and 2.

	Group 1	Group 2	p
Age (years)	73.69 ± 6.99	75.3 ± 6.48	NS
Sex (Female/Male ratio)	27/16	46/35	NS
Leukocyte count (10^3/mm^3)	13.63 ± 3.46	8.73 ± 3.34	<0.001
Neutrophil count (10^3/mm^3)	11.11 ± 3.26	6.24 ± 3.43	<0.001
Lymphocyte count (10^3/mm^3)	1.49 ± 0.95	1.71 ± 0.75	NS
Neutrophil/lymphocyte ratio	10.15 ± 6.7	5.78 ± 6.99	<0.001

NS= Non-significant



Area under the curve; area: 0.776, std.error: 0.043, asymptotic sig.: 0.000

Figure 1— ROC curve for NLR.

Significant differences were found between Groups 1 and 2 for leukocyte and neutrophil counts and NLR ($p<0.001$). No statistically significant differences were found for distribution of age, lymphocyte count, and gender.

ROC curve was drawn with existing data for NLR; when we take 3.93 for cut-off value sensitivity was %92.5 and specificity was %59.3 (Figure 1), when cut-off value was 4.51 sensitivity %87.5 and specificity %63, when cut-off value was 4.64 sensitivity %85 specificity %64.2 calculated (Table 2).

All patients aged over 65 who consulted to the intensive care unit with complaints of abdominal pain underwent whole abdominal ultrasonographic (US) and oral-intravenous-rectal contrast-enhanced whole abdominal computed-tomographic (CT) examinations. During radiological evaluation, an appendiceal diameter of more than 7 mm and presence of comorbidities (fluid collection, abscess, mesenteric contamination and free air) were accepted as positive findings suggestive of the presence of AA. In 10 cases evaluated by US in Group 1, appendiceal diameters were above 7 mm, and in the other cases appendices could not be visualized. On the computed-tomograms, appendiceal diameters were >7 mm (n=32), <7 mm (n=32), and in two cases concomitant pathologies were detected. In Group 2, US and CT imaging modalities did not reveal any findings that could explain the underlying pathology of the abdominal pain.

Table 2— Cut-off, Sensitivity, Specifity Values of NLR for ROC Curve.

Cut-off value	Sensitivity	Specificity	Sens. x Spes.
3.93	92.50	59.30	0.55
4.51	87.50	63.00	0.55
4.64	85.00	64.20	0.55

In the pathological evaluation of the 43 patients in Group 1, perforated (n=4), gangrenous and phlegmonous (n=36) and acute (n=3) appendicitis were detected.

Discussion

"Acute abdomen" is frequently encountered in intensive care units and despite developments in diagnostic and therapeutic methods, it still presents as a serious problem. It is not always possible for a surgeon to diagnose and treat a case of acute abdomen properly. AA is the most frequently seen etiological factor for acute abdomen. In infants, its incidence is relatively low, while it increases during childhood and reaches its maximum between 10 and 30 years of age. In all age groups its incidence is 7%, while perforation is seen in 17-20% of these cases (8).

In acute but uncomplicated cases of appendicitis, the patients usually present with leucocyte counts between 10000-18000/mm^3 and occasionally with moderate dominancy of polymorphonuclear leucocytosis (left shift). If white blood cell counts are within normal limits without left shift, then a diagnosis of acute appendicitis should be reconsidered. In uncomplicated cases of appendicitis, white blood cell counts (WBCs) rarely exceed 18000 /mm^3. If WBCs are above this level, then a perforated appendicitis or appendiceal abscess should be considered (8). In our study, whole blood cell counts were detected as follows: leukocyte count, Group 1=13.63±3.46 10^3/mm^3 and Group 2: 8.73±3.34 10^3/mm^3 ; neutrophil count, Group 1=11.11±3.26 and Group 2: 6.24±3.43 10^3/mm^3; and lymphocyte count, Group 1=1.49±0.95 10^3/mm^3 and Group 2=1.71±0.75 10^3/mm^3.

AA causes higher mortality rates in the elderly than in younger patients. Delay in diagnosis and treatment, and con-

comitant diseases, may be responsible for higher mortality rates in the elderly. The most important reason is delayed treatment. Classical signs in the elderly may not be so obvious. Signs on physical examination are usually very subtle. Abdominal distension is often seen. In 30% of elderly patients with AA, appendiceal perforation is detected intraoperatively. The most important factor in the development of perforation is delay in diagnosis and referral to a physician. Therefore in cases with presumptive AA, early surgical treatment is advised (9).

Acute appendicitis is likely to be an everyday occurrence in emergency units. Especially in rural areas, surgeons may not have imaging facilities. Further, the presence of ultrasonography or computed tomography imaging may not help in achieving an accurate diagnosis (10).

A study by Yazıcı et al. revealed that an NLR >3.5 has maximum sensitivity. They also indicated that higher N/L ratios have increased specificity and positive predictive value, while the most valuable results were obtained at NLR >5 (7). In 2014, Kahramanca et al. published a study that compared normal appendices with inflamed appendices and estimated the cut-off value of NLR as 4.68 (10). In complicated appendicitis, the cut-off value for NLR was estimated as 5.74, with a 70.8% sensitivity and 48.5% specificity. In limited number of published studies, a higher diagnostic value of NLR relative to conventional laboratory evaluations (leukocyte counts, C-reactive protein) has been indicated. In a study by Kahramanca et al., the researchers detected a diagnostic significance of NLR >4.68 for acute and NLR >5.74 for uncomplicated AA. However, normal ranges of NLR do not rule out a potential diagnosis of AA (10). Though in some publications higher cut-off values have been indicated, Ishizuka et al. detected a lower cut-off value for NLR. Ishizuka et al. reported a cut-off value for NLR of 8 in the differential diagnosis of gangrenous appendicitis (11).

In our study, NLR was found to be 10.15±6.7 and 5.78±6.99 in Groups 1 and 2, respectively. ROC curve for NLR; when we take 3.93 for cut-off value sensitivity was %92.5 and specificity was %59.3, when cut-off value was 4.51 sensitivity %87.5 and specificity %63, when cut-off value was 4.64 sensitivity %85 specificity %64.2 calculated. As it seen when cut-off value gets smaller it is more efficient to diagnose AA, when cut-off value gets bigger it is more efficient to diagnose nonsick patients. In our study 3.93 value has maximum sensitivity.

The usefulness of imaging techniques in the diagnosis of AA has been objectively demonstrated. However, the cost of imaging modalities apart from ultrasound and the excessive operator-dependent characteristics of ultrasound and its requirement for experience create difficulties. The reliability of ultrasound reportedly ranges between 71 and 95 percent (12). However, it has been recognized that overemphasizing the diagnostic value of ultrasound leads to an increase in the number of negative laparotomies, and it should not override clinical symptoms that are more valuable in the diagnosis of AA (13). In our study, in Group 1, the diameters of appendices were more than 7 mm as evaluated by ultrasonographic (US) examinations in 10 cases; in the other cases the appendices could not be visualized.

In a study by Kum et al., the authors found that appendectomies were performed on patients with normal (14%), inflammatory (70%) and perforated (16%) appendices (14). In our study, we found perforated (n=4), gangrenous and phlegmonous (n=36) and AA (n=3).

In the case of delayed intervention, clinical manifestations of simple appendicitis result in perforation, and the delay increases rates of mortality and morbidity. Therefore, the overall tendency in surgical clinics is to operate the patient before establishing signs and symptoms. For that reason, decisions to operate result in the removal of normally appearing appendices in 15-30% of cases. Increased rates of negative laparotomy can be reduced with an increase in the observation period; however, this can result in the development of a perforation, which can increase morbidity and mortality rates. The use of adjunctive diagnostic methods might decrease the number of unnecessary operations, perforation rates and length of hospital stay (15,16).

When compared with the last century, a pronounced drop in morbidity and mortality can be seen to stem from an aggressive surgical strategy. Consequently, negative appendectomy rates approaching 30% are generally accepted all over the world (17). As the negative appendectomy rates increase, perforation rates decrease proportionally. The mean perforation rate is 3.6% in young men and higher in children and the elderly (18).

In conclusion, frequently used laboratory tests do not suffice to establish a definite diagnosis of AA in cases over 65 years of age. Preoperatively estimated NLR can be accepted as easily available, adjunctive data with a lower cost, contributing to the diagnosis of AA.

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