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CLINICAL RESEARCH / KLİNİK ARAŞTIRMA

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Rising Incidence of Incidental Appendiceal Neoplasms and Complicated Appendicitis in the Geriatric Population: Predictive Performance of the HALP Score and the Systemic Immune-inflammation Index (SIII)

Geriatrik Popülasyonda İnsidental Apendiks Neoplazmlarının ve Komplike Apandisitin Artan İnsidansı: HALP Skorunun ve Sistemik İmmün-inflamasyon İndeksinin (SIII) Prediktif Performansı

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Abstract

Objective: To assess the frequency and predictive performance of clinicopathological factors associated with for incidental appendiceal neoplasms and complicated appendicitis in the geriatric population.

Methods: Adult appendectomy cases (≥18 years) performed from 2016 to 2024 were retrospectively reviewed. Age-based grouping classified patients as non-geriatric (18-64 years) or geriatric (≥65 years). Demographic data, laboratory findings, appendicitis type, and histopathology were recorded.

Results: Of the 859 patients, 16.3% were geriatric. Complicated appendicitis occured at a higher rate in geriatric group (31.1% vs. 12.5%; p<0.001). Incidental neoplasms were identified in 29 of 859 patients (3.4%). Detection was markedly more frequent in the ≥65 age group (15.0%) than in younger patients (1.1%; p<0.001). Malignant tumors accounted for 4.3% of cases in older patients, compared with 0.6% in the younger group (p=0.002). Age was independently associated with the presence of neoplasm (p<0.001). Receiver operating characteristic analysis supported an age threshold of 61 years, with an area under the curve of 0.87 (sensitivity, 79.3%; specificity, 83.1%).

Conclusion: Advanced age increases the risk of neoplasia and of a complicated clinical course in acute appendicitis. Clinical decisions should be individualized by taking into account age, clinical and radiological findings, and multiple inflammatory markers.

Keywords: Acute appendicitis, geriatric population, appendiceal neoplasms, complicated appendicitis

Öz

Amaç: Geriatrik popülasyonda tesadüfi apendiks neoplazileri ve komplike apandisit için klinikopatolojik parametrelerin sıklığını ve öngörü değerini değerlendirmek.

Yöntem: 2016-2024 yılları arasında bir üçüncü basamak sağlık merkezinde apendektomi uygulanan ≥18 yaş hastalar retrospektif olarak incelendi. Hastalar geriatrik olmayan (18-64 yaş) ve geriatrik (≥65 yaş) olmak üzere iki gruba ayrıldı. Demografik veriler, laboratuvar bulguları, apandisit tipi ve histopatoloji sonuçları kaydedildi.

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Öz

Bulgular: Toplam 859 hastanın %16,3'ü geriatrikti. Komplike apandisit, geriatrik grupta daha sık görüldü (%31,1'e karşı %12,5; p<0,001). Genel neoplazi oranı %3,4 (29/859) olup geriatrik hastalarda anlamlı derecede yüksekti (%15,0'a karşı %1,1; p<0,001). Malignite oranları ise sırasıyla %4,3 ve %0,6 idi (p=0,002). Yaş, neoplazi varlığı ile bağımsız olarak ilişkili bulundu (p<0,001). Alıcı işletim karakteristiği analizinde optimal eşik değer 61 yaş olarak hesaplandı (eğri altında kalan alan: 0,87, duyarlılık: %79,3, özgüllük: %83,1).

Sonuç: İleri yaş, akut apandisitte neoplazi ve komplike seyir riskini artırmaktadır. Klinik kararlar; yaş, klinik ve radyolojik bulgular ile birden fazla inflamatuvar belirteç birlikte değerlendirilerek bireyselleştirilmelidir.

Anahtar Kelimeler: Akut apandisit, geriatrik popülasyon, apendiks neoplazm, komplike apandisit

Introduction

Appendiceal neoplasms (AN) are rare entities, with a substantial proportion diagnosed incidentally during routine histopathological examination following appendectomy[1]. They account for less than 0.5% of all gastrointestinal malignancies and have historically been reported in approximately 1% of appendectomy specimens[2]. However, recent reports describe higher detection rates of AN, likely influenced by more comprehensive pathological examination of resected specimens[3-5].

ANs encompass a wide histopathological spectrum, including well-differentiated neuroendocrine tumors (NETs), low- and high-grade mucinous neoplasms, and adenocarcinomas[3]. While NETs predominantly occur in younger individuals and tend to be small and localized, mucinous neoplasms and adenocarcinomas are more common in older populations and may exhibit a more aggressive clinical course[4].

The clinical presentation of ANs is often non-specific; patients usually have either classic symptoms of acute appendicitis or non-specific abdominal pain. Therefore, even in routine cases of appendicitis, a meticulous histopathological assessment is essential to detect underlying malignancies[5]. The incidence of ANs increases with age, particularly in patients over 50 presenting with appendicitis[3,4]. Furthermore, the increasing adoption of non-operative management strategies for appendicitis raises additional concerns regarding the risk of missed occult neoplasms[5].

The limited availability of reliable clinical markers other than age and imaging findings has increased interest in hematological and biochemical composite indicators. In this context, parameters such as the hemoglobin, albumin, lymphocytes, platelets (HALP) score and the systemic immune-inflammation index (SIII) are valuable in predicting complications and prognosis in gastrointestinal tract tumors. Lower HALP scores are thought to indicate compromised nutritional reserve alongside systemic inflammation, and have been correlated with poorer prognosis[6,7]. Nonetheless, the clinical utility of these indices in ANs remains poorly defined. Particularly in the elderly, these biomarkers may facilitate earlier recognition of ANs and their aggressive subtypes.

In this study, we explored the occurrence and pathological spectrum of incidental appendiceal tumors among elderly individuals and examined whether HALP and SII provide meaningful predictive information in this setting.

Materials and Methods

This retrospective cohort comprised adult patients who were treated with appendectomy between 2016 and 2024 at the Department of General Surgery, Aydın Adnan Menderes University. Eligibility was restricted to individuals aged 18 years or above. Only cases with confirmed histopathological findings were analyzed, while negative appendectomy specimens were excluded. For comparative analysis, participants were stratified by age into non-geriatric (18-64 years) and geriatric (≥65 years) categories.

Demographic characteristics (age, sex), laboratory parameters [white blood cell count, neutrophils, lymphocytes, platelets, C-reactive protein (CRP), hemoglobin, albumin], histopathological findings, the type of appendicitis (complicated or uncomplicated), and the presence and subtypes of neoplasms were retrospectively retrieved from hospital records and patient charts.

The following formula was used for biomarker calculation: HALP score=hemoglobin (g/L)×albumin (g/L)×lymphocyte count ($\times 10^9$/L)÷platelet count ($\times 10^9$/L). SIII=neutrophil count ($\times 10^9$/L)×platelet count ($\times 10^9$/L)÷lymphocyte count ($\times 10^9$/L). Appendicitis was classified as complicated when perforation, abscess formation, or gangrene were identified.

The research ethics approval was obtained from the Ethical Review Board of the Aydın Adnan Menderes University

Ethical Committee (approval no: 2025/284, date: 02.10.2025). The study was performed in compliance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants for the use of their clinical data and protected health information.

Statistical Analysis

Statistical analyses were performed with IBM SPSS Statistics (26.0; IBM Corp., Armonk, NY, USA). Normality of continuous variables was evaluated using the Kolmogorov-Smirnov and Shapiro-Wilk tests. Continuous data are reported as mean ± standard deviation when normally distributed, and as median (range) otherwise. Categorical variables are presented as numbers and percentages. Between-group comparisons were performed using the chi-square test or Fisher's exact test for categorical variables, and Student's t-test or the Mann-Whitney U test for continuous variables, depending on the distribution. Predictor candidates that showed significance in univariate testing and were deemed clinically meaningful were examined using receiver operating characteristic (ROC) curve analysis, with area under the curve (AUC) estimates reported. Where applicable, effect sizes are provided alongside 95% confidence intervals (CIs). The optimal cut-off value was selected based on the Youden index. A p-value of <0.05 was considered statistically significant in all analyses.

Results

Between 2016 and 2024, 870 appendectomies were performed at our tertiary referral center. Histopathological analysis revealed negative appendectomies in 11 cases (1.3%), with comparable rates between groups (p=0.1703). After excluding these cases, the final cohort consisted of 859 patients: 140 (16.3%) were geriatric and 719 (83.7%) were non-geriatric. The overall mean age was 43.6 years. The mean age in the geriatric group was 71.7 years (65-91), while it was 38.1 years (18-62) in the non-geriatric group. In the overall cohort, men accounted for 56.2% and women for 43.8%. The incidence of complicated appendicitis was more often in the geriatric group (31.1%) than the non-geriatric group (12.5%) (p<0.0001). The overall incidence of incidental AN was 3.4% (29/859). Among these, 65.5% (n=19) were benign and 34.5% (n=10) were malignant. Incidental neoplasms were more often detected in geriatric group (15.0%) than in non-geriatric group (1.1%) (p<0.0001). Malignant tumors were detected in 1.2% of the total cohort and was more common in geriatric group (4.3%) than in non-geriatric group (0.6%) (p=0.002). Among the 29 patients diagnosed with neoplasms, the most common neoplasm was low-grade appendiceal mucinous neoplasm (LAMN), accounting for 41.4%. In both age groups, LAMN was the most frequent benign subtype, whereas NET was the most common malignant subtype (Table 1).

Logistic regression,advancing age was independently associated with AN [odds ratio (OR)=1.09, 95% CI: 1.06-1.12; p<0.001]. Age showed substantial discriminative ability for neoplasm detection in ROC analysis (AUC: 0.87). An age threshold of 61 years provided optimal discrimination (sensitivity 79.3% and specificity 83.1%) (Figure 1). Figure 2 displays the age distribution of patients diagnosed with incidental neoplasms.

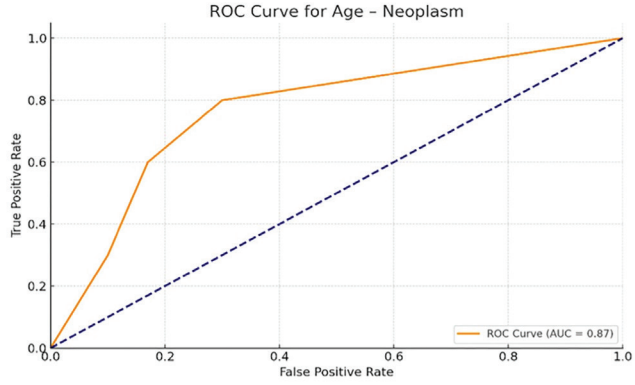

Figure 1. Receiver operating characteristic (ROC) curve illustrating the diagnostic performance of age for predicting neoplasm. The area under the curve (AUC) indicates age's discriminatory ability to distinguish between patients with and without neoplasm

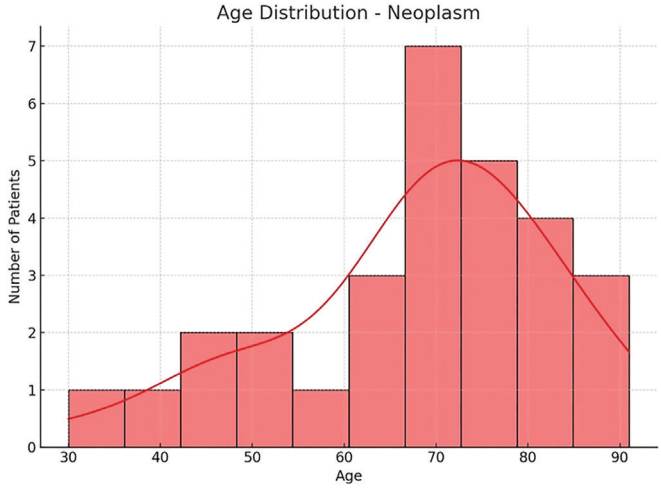

Figure 2. Age distribution among patients with appendiceal neoplasm. Histogram showing the frequency of patients according to age groups

Among geriatric patients, inflammatory markers differed significantly between complicated and uncomplicated appendicitis. CRP, neutrophil count, and SII values were higher in patients with complicated appendicitis (p<0.001, p=0.047, and p=0.008, respectively). Conversely, HALP scores were lower in complicated cases (p=0.007) (Table 2). ROC analysis was performed to evaluate how well laboratory parameters discriminated complicated appendicitis. CRP emerged as the most powerful biomarker (AUC: 0.748, p<0.001), demonstrating good discriminative ability. SII showed a moderate diagnostic performance (AUC: 0.652, p<0.001). In contrast, the HALP score (AUC: 0.345, p=0.814) exhibited poor diagnostic accuracy, limiting its utility as an independent clinical predictor (Table 3). The ROC curves for complicated vs. non-complicated cases in the geriatric group are displayed in Figure 3. In the ROC curve analysis to predict the presence of a neoplasm, none of the parameters showed significant discrimination (p>0.05).

Discussion

Although incidental ANs are rare in patients undergoing appendectomy for acute appendicitis, they hold substantial clinical significance. In most cases, the diagnosis is not anticipated preoperatively and is instead made through postoperative histopathological analysis. Earlier reports was reported AN incidence rates ranging from 0.5% to 2.5%[8-10]. However, the incidence has been reported to be higher in current studies than in previous literature. Dohner et al.[11] reported a 3.7% rate of neoplasms in a retrospective single-center study, while Gómez Báez et al.[12] reported a 3.2% rate. Our study was consistent with this pattern and detected neoplasms at a rate of 3.4%.

The presence of incidental ANs in elderly patients has been a matter of long-standing debate in the literature. Advanced age represents a significant predisposing factor for underlying neoplasia in patients presenting with acute appendicitis. Numerous recent chorts have demonstrated a marked rise in the likelihood of tumor detection with advancing age[8,13-18]. Fransvea et al.[19] reported neoplasia rates of 13% among individuals over 40 years, compared to only 3.8% in those under 30. Our findings align with this evidence, revealing a significantly higher rate of neoplasms in the geriatric group (15.0% vs. 1.1%, p<0.0001). Malignancy was more frequent in the elderly (4.3% vs. 0.6%, p=0.002). Higher age corresponded

Table 1. Baseline characteristics and histopathological diagnoses

	All, n (%)	Geriatric, n (%)	Non-geriatric, n (%)	p-value
Number	859	140	719	
Negative appendectomy	11 (1.3%)	4 (2.8%)	7 (1.0%)	0.17
Age				
Mean ± SD	43.6±16.4	71.7±6.9	38.1±11.3	
Median	40 (18-91)	70.0 (65-91)	36.0 (18-62)	
Sex				
Male	489 (56.2%)	72 (50.3%)	417 (57.4%)	0.146
Female	381 (43.8%)	71 (49.7%)	310 (47.6%)	
Non-complicated	704 (84.8%)	82 (68.9%)	622 (87.5%)	<0.001
Complicated	126 (15.2%)	37 (31.1%)	89 (12.5%)	
Incidental neoplasm	29 (3.4%)	21 (15%)	8 (1.1%)	<0.001
Benign	19 (2.2%)	15 (10.7%)	4 (0.5%)	<0.001
Malign	10 (1.2%)	6 (4.3%)	4 (0.6%)	0.002
Histology of neoplasms				
LAMN	12 (41.4%)	8 (38.1%)	4 (50.0%)	
Serrated adenoma	6 (20.7%)	6 (28.6%)	0 (0.0%)	
Hyperplastic polyp	1 (3.4%)	1 (4.8%)	0 (0.0%)	
NET	4 (13.8%)	2 (9.5%)	2 (25.0%)	
Adenocarcinoma	3 (10.3%)	2 (9.5%)	1 (12.5%)	
Mucinous adenocarcinoma	2 (6.9%)	1 (4.8%)	1 (12.5%)	
Signet-ring cell carcinoma	1 (3.4%)	1 (4.8%)	0 (0.0%)	

LAMN: Low-grade appendiceal mucinous neoplasm, NET: Neuroendocrine tumor, SD: Standard deviation

to greater odds of neoplasia (OR=1.09; 95% CI: 1.06-1.12; p<0.001), and ROC analysis confirmed a strong discriminative performance (AUC: 0.87), with 61 years identified as the optimal cut-off. These findings highlight the need to keep underlying neoplasia in elderly patients presenting with acute appendicitis. Even in available literature supporting non-operative approaches, the risk of missed malignancy ranges from 0.7% to 2.5%[11]. In patients aged ≥65 managed conservatively, this incidence was reported to reach 3.9%[17]. Therefore, the diagnostic and therapeutic advantages of appendectomy should be strongly considered, especially in geriatric patients and in those with high clinical and imaging suspicion. Notably, our data showed that the rate of negative appendectomy did not increase in elderly patients (p=0.1703), suggesting that concerns about "unnecessary surgery" in this population may be overstated. Conversely, diagnostic delays may pose greater risks, including disease complications and undetected malignancy.

AN exhibit a broad histopathological spectrum. LAMNs a are frequently encountered among benign or premalignant neoplasms, whereas NETs are most prevalent among malignant types[8,20-23]. Consistent with the literature, our series showed that the majority of benign and premalignant neoplasms were LAMNs, whereas NETs and adenocarcinomas were the most common malignant subtypes. Although our data and prior reports indicate that a significant portion of ANs are low-grade or have limited malignant potential, the risk of invasive cancer should not be underestimated.

Table 2. Comparison of biomarkers in complicated vs. non-complicated acute appendicitis in geriatric patients

Parameter	Complicated	Non-complicated	p-value
White blood cell count (×10³/µL)			
Mean ± SD	14.45 (6.66)	12.43 (4.58)	0.056
Median (min-max)	13.14 (2.82-31.47)	11.66 (4.57-24.27)	
Neutrophil count (×10³/µL)			
Mean ± SD	12.33 (6.29)	9.93 (4.47)	0.047
Median (min-max)	11.31 (2.21-29.99)	9.23 (2.73-21.55)	
Lymphocyte count (×10³/µL)			
Mean ± SD	1.31 (0.65)	1.55 (0.87)	0.319
Median (min-max)	1.21 (0.21-2.56)	1.38 (0.43-5.30)	
Platelet count (×10³/µL)			
Mean ± SD	280.05 (96.99)	247.70 (79.01)	0.067
Median (min-max)	254.00 (144.00-640.00)	231.50 (100.00-519.00)	
C-reactive protein (mg/L)			
Mean ± SD	178.90 (94.66)	91.76 (89.02)	<0.001
Median (min-max)	178.00 (2.00-332.70)	63.00 (2.00-363.19)	
Albumin (g/L)			
Mean ± SD	36.72 (4.79)	37.91 (5.13)	0.15
Median (min-max)	37.00 (26.90-45.00)	38.20 (22.00-49.00)	
Hemoglobin (g/dL)			
Mean ± SD	12.13 (1.93)	12.73 (1.73)	0.094
Median (min-max)	12.00 (7.80-16.10)	12.70 (7.00-15.80)	
SII			
Mean ± SD	3010.08 (2204.25)	2102.77 (1728.87)	0.008
Median (min-max)	2312.43 (430.81-9617.48)	1635.22 (164.63-9222.72)	
HALP score			
Mean ± SD	22.1 (12.9)	33.1 (21.7)	0.007
Median (min-max)	20.8 (3.7-51.1)	28.0 (4.7-104.2)	

HALP score: Hemoglobin (g/L)×albumin (g/L)×lymphocyte count (×10⁹/L)÷platelet count (×10⁹/L), SII: Systemic immune-inflammation index: neutrophil count (×10⁹/L)×platelet count (×10⁹/L)÷lymphocyte count (×10⁹/L), SD: Standard deviation

Table 3. ROC curve analysis of biomarkers for predicting the difference between complicated and non-complicated acute appendicitis in geriatric patients

Parameter	AUC (95% CI)	Cut-off	Sensitivity	Specificity	PPV	NPV	p-value
C-reactive protein (mg/L)	0.748 (0.639-0.838)	>147.2	70.3% (54.2-82.5)	75.6% (65.3-83.6)	56.5% (42.2-69.8)	84.9% (75.0-91.4)	<0.001
White blood cell	0.588 (0.471-0.695)	>12.4	67.6% (51.5-80.4)	56.1% (45.3-66.3)	41% (29.5-53.5)	79.3% (67.2-87.7)	0.067
Neutrophil count ($\times10^3/\mu L$)	0.614 (0.499-0.723)	>9.13	75.7% (59.9-86.6)	48.8% (38.3-59.4)	40.0% (29.3-51.7)	81.6% (68.6-90.0)	0.027
Platelet	0.605 (0.494-0.707)	>227.0	81.1% (65.8-90.5)	47.6% (37.1-58.2)	41.1% 30.5-52.6)	84.8% (71.8-92.4)	0.03
SII	0.652 (0.557-0.746)	>1394.0	86.5% (72.0-94.1)	45.1% (34.8-55.9)	41.6% (31.2-52.7)	88.1% (75.0-94.8)	<0.001
HALP score	0.345 (0.246-0.456)	<19.3	84.2% (62.4-94.5)	20.0% (10.5-34.8)	33.3% (21.7-47.5)	72.7% (43.4-90.3)	0.814

Cut-off values were determined according to the Youden index

ROC: Receiver operating characteristic, AUC: Area under the curve, CI: Confidence interval, PPV: Positive predictive value, NPV: Negative predictive value, HALP score: Hemoglobin (g/L)×albumin (g/L)×lymphocyte count ($\times10^9$/L)÷platelet count ($\times10^9$/L), SII: Systemic immune-inflammation index: neutrophil count ($\times10^9$/L)×platelet count ($\times10^9$/L)÷lymphocyte count ($\times10^9$/L)

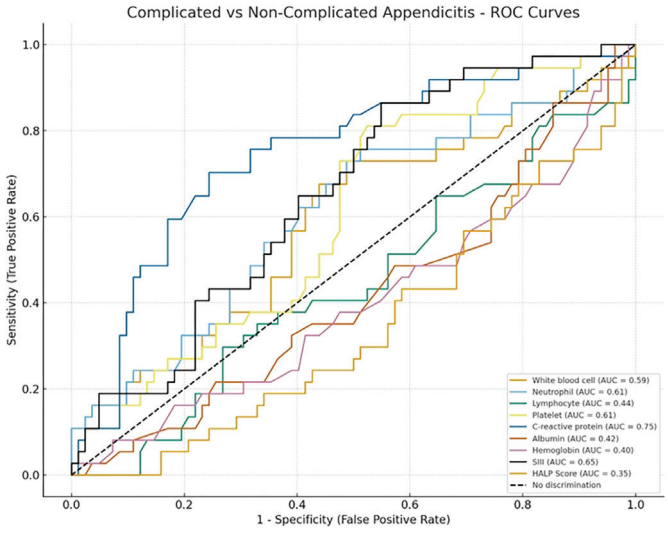

Figure 3. Receiver operating characteristic (ROC) curves of biomarkers for predicting complicated and non-complicated acute appendicitis in geriatric patients. The area under the curve (AUC) indicates the ability of these biomarkers to discriminate between the two patient groups

SII: Systemic immune-inflammation index, HALP: Hemoglobin, albumin, lymphocytes, platelets

In acute appendicitis, CRP has long been used as a marker associated with disease severity[19]. Recently, additional indices, including SIII and HALP scores, were evaluated in this context[24,25]. In our study, the incidence of complicated appendicitis was higher in geriatric patients than in non-geriatric patients (31.1% vs. 12.5%; p<0.0001). Among geriatric patients with complicated appendicitis, CRP, neutrophil count, and SIII values were higher than in uncomplicated cases (p<0.001, p=0.0479, and p=0.0083, respectively). The HALP score was notably lower (p=0.007). In ROC analysis, CRP demonstrated the strongest diagnostic performance (AUC: 0.744; p<0.001). SIII (AUC: 0.672; p=0.007) demonstrated moderate discriminatory ability. Although complicated cases were characterized by lower HALP scores (p=0.007), the ROC performance was limited (AUC: 0.339; p=0.0028). These results support the use of combined inflammatory markers rather than reliance on a single parameter to improve clinical accuracy. However, none of the biomarkers studied exhibited significant predictive value for AN (p>0.05).

Study Limitations

A number of limitations should be acknowledged. Most notably, the retrospective, single-center nature of the study may have increased the risk of selection bias. In addition, changes in pathology sampling protocols and reporting standards between 2010 and 2024 may have caused measurement inconsistencies. The absence of long-term oncologic outcomes limits the interpretation of prognostic implications.

Acute appendicitis in elderly patients may exhibit distinct biological behavior. Age should be recognized as a major

determinant of AN. Each case of appendicitis in an elderly patient must be approached as a potential neoplasm, with surgical and follow-up strategies tailored accordingly. Therefore, in elderly patients with diagnostic uncertainty, early surgical intervention should be strongly considered. This approach will facilitate the timely diagnosis of potentially occult neoplasms. Our findings, consistent with the current literature, support a more aggressive approach to the management of acute appendicitis in elderly individuals. Considering that the histopathological spectrum of ANs mostly consists of lesions with a better prognosis, appendectomy may provide adequate treatment in many cases. However, the need for additional oncologic treatment is more likely in the geriatric population.

Conclusion

Both our data and the current literature indicate that the likelihood of neoplasia and complicated disease is markedly higher among elderly patients with acute appendicitis. Management strategies should be planned, taking this reality into account. Even when considering non-operative approaches, the potential for underlying malignancy must be carefully assessed. Personalized treatment decisions should incorporate patient age, clinical and radiological findings, and laboratory profiles. Prospective multicenter cohorts are warranted to strengthen clinical decision-making algorithms.

Ethics

Ethics Committee Approval: The research ethics approval was obtained from the Ethical Review Board of the Aydın Adnan Menderes University Ethical Committee (approval no: 2025/284, date: 02.10.2025).

Informed Consent: Written informed consent was obtained from all participants for the use of their clinical data and protected health information.

Footnotes

Authorship Contributions

Surgical and Medical Practises: O.A., E.B.C., M.Ç.C., S.A., A.E., Concept: O.A., E.B.C., Design: O.A., Data Collection or Processing: O.A., E.B.C., M.Ç.C., S.A., A.E., Analysis or Interpretation: E.B.C., M.Ç.C., S.A., A.E., Literature Search: O.A., M.Ç.C., S.A., A.E., Writing: O.A.

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

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