

# Determination of factors associated with perforation in patients with geriatric acute appendicitis

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## ABSTRACT

**BACKGROUND:** Recognition and management of abdominal emergencies in geriatric patients are more complicated compared to the younger population. We aimed to investigate the demographic characteristics of geriatric patients diagnosed with acute appendicitis and to investigate the factors associated with perforation in the early stages in this study.

**METHODS:** After obtaining local ethical committee approval, patients 65 years and older who had appendectomy between January 2015 and December 2019 were included the study. Demographic data of the patients, physical examination findings, and laboratory results were analyzed. Patients were divided into two groups based on surgical reports: Perforated and simple appendicitis.

**RESULTS:** During the study period, 72 patients were evaluated. In our study, 48.6% of the patients were male, and the median age was 71.5 years (IQR 25–75, 68–80). Perforated appendicitis was detected in 28% of the patients. We were determined that the vast majority of patients with perforated appendicitis were male; had more frequent chronic kidney disease and post-operative local complications; had increased leukocytes, neutrophils, blood urea nitrogen, creatinine, and total bilirubin; and had reduced albumin; and these differences were statistically significant (all values  $p < 0.05$ ). Multivariate analysis shows increased neutrophil count and male sex was significantly associated with perforated appendicitis ( $p = 0.035$  and  $p = 0.01$ , respectively).

**CONCLUSION:** Geriatric patients with chronic kidney disease can be at higher risk of perforated appendicitis due to inadequate abdominal physical examination results. In addition, male gender and an elevated neutrophil count are independent predictors of perforation.

**Keywords:** Acute appendicitis; geriatric; perforation.

## INTRODUCTION

Abdominal pain in geriatric patients is the third most frequent reason for admission to the emergency room after chest pain and shortness of breath.<sup>[1]</sup> Recognition and management of abdominal emergencies in geriatric patients is more complicated compared to the younger population.<sup>[2]</sup> Geriatric patients admitted to the emergency room because of abdominal pain have up to 60% higher hospitalization rates and longer hospitalization durations.<sup>[1,3]</sup> Approximately 20% of geriatric patients admitted because of abdominal pain undergo an invasive surgery.<sup>[4]</sup> With aging, a large number of physiological changes occur in geriatric patients; a decrease in colonic motility and transition

time as well as dysfunction of the pelvic floor leads to more frequent constipation in this age group.<sup>[4,5]</sup> Abdominal examination in the elderly can be variable. Rebound sensitivity due to atrophy in the abdominal muscles may decrease, and changes in the response of the nervous system due to aging lead to changes in the detection and limitation of pain; thus, it can delay the occurrence of diseases and make abdominal problems difficult to detect by physical examination. Morbidity and mortality are higher in the geriatric population than that in the younger population because of decreased system functions, worsening nutrition, concomitant diseases, and polypharmacy.<sup>[1,2,6]</sup>

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Acute appendicitis is a common disease under emergency abdominal surgery. Geriatric patients account for only 5–10% of all cases of appendicitis; however, their mortality rate is 5–8 times higher than that of younger patients. In patients aged >60 years, classical signs of appendicitis were present in only 10–20% of patients.<sup>[4,5,7]</sup> Moreover, approximately 25% of patients may not have sensitivity in the right lower quadrant. Studies have shown that it is relatively difficult to diagnose appendicitis clinically in geriatric patients.<sup>[5,7]</sup>

Studies in the literature have suggested that geriatric patients with acute appendicitis are admitted to the hospital later compared to younger people, and this delay is one of the factors that contribute to the high incidence of perforating appendicitis in geriatric patients.<sup>[5,7,8]</sup> Changes in physical examination findings in geriatric patients, concomitant diseases, delay in hospitalization, atypical clinical findings, and advanced age may cause longer hospitalization. Determining factors associated with perforation in geriatric patients diagnosed with acute appendicitis may be useful in the early identification of patients at risk for perforation and mortality, and a reduction in mortality and post-operative complications may be achieved.

The purpose of our study was to investigate the demographic characteristics of geriatric patients diagnosed with acute appendicitis and to investigate the factors associated with perforation in the early stages.

## MATERIALS AND METHODS

### Study Design

Our retrospective study was conducted in a tertiary care ED with approximately 250,000 patient admissions per year. Before implementation, our study's protocol was approved by the local ethics committee. As this is a retrospective study, the participants' informed consent was not required.

### Study Population

Patients aged  $\geq 65$  years that were admitted to the emergency department between January 1, 2015, and November 1, 2019, and were diagnosed with appendicitis pathologically following the after operation were included in the study.

Demographic data of the patients, comorbid diseases, time of admission to the hospital, period of hospitalization, time of the operation, previous surgical interventions, vital signs, physical examination findings, laboratory consultations (complete blood count, biochemical parameters, and coagulation tests), and post-operative complications, if any (local and systemic), were obtained from patient files by retrospective screening. Patients with incomplete data and patients without appendicitis based on the pathological report were excluded from the study.

Patients were divided into two groups based on surgical reports: Perforated and simple appendicitis. The appendix was considered perforated if there was free rupture of intraluminal contents.

### Surgical Technique

Laparoscopic appendectomy was standardized and used for all of the patients. Standard three-port technique was used and 10 mm trocar was placed just below the umbilicus for camera. Five millimeters port was placed 10 cm below the umbilicus and 10 mm port was placed 10 cm above the umbilicus, all on the midline. After creating pneumoperitoneum, appendix vermiformis was holds on the distal end by a grasper and suspended. Without separating appendix from mesoappendix like it is performed on standard open or laparoscopic technique, we used 3.5 mm linear stapler to transect the appendiceal stump from cecum with a safety margin. Then, the resected appendix stump was evaluated for bleeding and inadequate incision after the bleeding control; stump was scrubbed with povidone-iodine in all cases. Appendectomy specimen was removed through the 10 mm port in an endobag. Intravenous metronidazole was administered to all of the patients preoperatively. One Hemovac drain was placed through the 5 mm trocar to patients with perforated appendicitis and the procedure was finalized after hemostasis.

### Statistical Analysis

Data analysis was performed using SPSS for Windows 16. The normality of the distribution of the discrete and continuous variables was checked using the Kolmogorov–Smirnov test. Descriptive statistics included numbers and percentages for qualitative variables and medians (interquartile range 25–75) for discrete and continuous variables. Categorical variables were compared using the Chi-square test and continuous variables with the Mann–Whitney U-test. Predictors of perforation of appendix were determined using univariate tests, and statistically significant ( $p < 0.2$ ) variables were tested with a multivariate logistic regression model. The fitness of this model was tested with the Hosmer–Lemeshow test.

$P < 0.05$  was considered to be statistically significant.

## RESULTS

During the study period, 83 patients were identified. A total of 11 patients with incomplete data were excluded from the study, and 72 patients were included in the study. In our study, 48.6% of the patients were male, and the median age was 71.5 years (IQR 25–75, 68–80). The most common comorbid disease in the patients was hypertension. Abdominal pain (94.4%) was the most frequent complaint for admission to the emergency service, and 86.1% of the patients had sensitivity in the right lower quadrant based on abdominal examinations. Perforated appendicitis was detected in 28% of the patients. Demographic data of the patients are shown in Table 1.

**Table 1.** Demographic data of patients (n=72)

Sex n (%)	
Male	35 (48.6)
Age, years, median (IQR 25-75)	71.5 (68–80)
Comorbidity, n (%)	
Hypertension	34 (47.2)
Diabetes Mellitus	13 (18.1)
Coronary heart disease	14 (19.4)
Chronic heart failure	3 (4.2)
Chronic renal failure	6 (8.3)
COPD	10 (13.9)
Admitting time, n (%)	
08.00–17.00	33 (45.8)
17.00–08.00	35 (54.2)
Previously surgery, n (%)	10 (13.9)
Complaints, n (%)	
Abdominal pain	68 (94.4)
Nausea and / or vomiting	64 (88.9)
High temperature	13 (13.9)
Sensitivity in the right lower quadrant	62 (86.1)
Imaging, n (%)	
Ultrasonography	34 (47.2)
Computed tomography	40 (55.6)
Retrocecal appendicitis, n (%)	3 (4.2)
Perforation, n (%)	20 (27.8)
Post operative systemic complications, n (%)	
Respiratory failure	2 (2.8)
Pneumonia	1 (1.4)
Post operative local complications, n (%)	
Wound separation	8 (11.1)
Peritonitis	7 (9.7)
Bowel obstruction	0 (0)
Laboratory, median (IQR 25–75)	
Hemoglobin g/dL	13.5 (12.5–14.6)
White blood cell ( $10^3/\mu\text{L}$ )	13.6 (10.7–17.5)
Neutrophil ( $10^3/\mu\text{L}$ )	11.4 (8–14.8)
Lymphocytes ( $10^3/\mu\text{L}$ )	1.4 (1.04–2.1)
Platelet ( $10^3/\mu\text{L}$ )	235 (190–290)
INR	1.19 (1.06–1.26)
Glucose (mg/dL)	133 (113–178)
BUN (mg/dL)	16 (14–21.8)
Creatinine (mg/dL)	1 (0.8–1.24)
Albumin (g/dL)	3.5 (3–4.1)
Total Bilirubin (mg/dL)	1.03 (0.7–1.55)
Hospital stay duration, (days) median (IQR 25–75)	5 (3–6.7)
Time to surgery from pain starting, (hours) median (IQR 25–75)	13.2 (12–17)

COPD: Chronic obstructive pulmonary disease; BUN: Blood Urea Nitrogen; INR: International normalized ratio.

When patients with perforated appendicitis were compared with non-perforated ones, it was determined that the vast majority of patients with perforated appendicitis were male; had more frequent chronic kidney disease (CKD) and post-operative local complications; had increased leukocytes, neutrophils, blood urea nitrogen (BUN), creatinine, and total bilirubin; and had reduced albumin; and these differences were statistically significant (all values  $p < 0.05$ ) (Table 2).

Multivariate logistic regression analysis was performed to examine the effects of variables examined in Table 2 with other variables. As CKD, BUN, and albumin levels correlated with creatinine, leukocyte, lymphocyte, and neutrophil count, they were not included in the model. The multivariate model included the neutrophil count with  $p \leq 0.2$  in Table 2, duration of pain till the operation, creatinine level, bilirubin level, and age and gender. Once it was observed that the established model was fit based on Hosmer-Lemeshow test, it was noted that increased neutrophil count and male sex were significantly associated with perforated appendicitis ( $p = 0.035$  and  $p = 0.01$ , respectively) (Table 3).

## DISCUSSION

Acute appendicitis is a significant emergency, especially in the geriatric age group, and mortality and morbidity are higher than that in the younger people. The aim of the present study was to investigate the factors associated with perforation in geriatric patients diagnosed with acute appendicitis, and it was determined that the perforation rate was 28% and that the perforation risk was higher in male patients and high neutrophil count patients.

Clinical diagnosis of appendicitis in geriatric patients is more difficult compared to younger people.<sup>[9]</sup> Pain sensations also change because of changes in nerve conductions due to aging. Thus, clinical manifestations can be atypical and mild, and typical clinical manifestations of appendicitis are detected in a small number of geriatric patients.<sup>[10,11]</sup> The probability of perforation of appendicitis depends on a wide range of pathogenic and morphological factors. In geriatric patients, the incidence of perforated appendicitis was 32–50% mainly due to inadequate anamnesis and delayed diagnosis caused by physical examination.<sup>[7,12,13]</sup> The perforation rate in our study was 28%. This rate is relatively low compared to the rates in the literature. This may be due to the close proximity of our hospital to settlements and the ease of transportation and low thresholds of admissions to emergency services in Turkey. In our study, univariate analyses showed that the vast majority of patients with perforated appendicitis were male, had more common CKD and post-operative local complications, had a higher leukocyte and neutrophil count, and had a lower lymphocyte count. The study by Sheu et al.<sup>[8]</sup> suggested that the perforation rate in men is approximately twice as high as women, and this may have resulted from the cultural reluctance of older men about seeking medical care in their

**Table 2.** Comparison of patient characteristics and comorbidity factors between patients with perforated and non-perforated appendicitis

Characteristics	Perforated (n=20)	Non-Perforated (n=52)	p-value
Sex, n (%)			
Male	15 (75)	20 (38.5)	0.005
Age, years, median (IQR 25–75)	73 (67–79.7)	71 (68–80)	0.890
Comorbidity, n (%)			
Hypertension	8 (40)	26 (50)	0.446
Diabetes Mellitus	4 (20)	9 (17.3)	0.790
Coronary heart disease	2 (10)	12 (23.1)	0.322
Chronic heart failure	0 (0)	3 (5.8)	0.555
Chronic renal failure	5 (25)	1 (1.9)	0.005
Chronic obstructive pulmonary disease	3 (15)	7 (13.5)	0.866
Admitting time, n (%)			
08.00–17.00	9 (45)	24 (46.2)	0.930
17.00–08.00	11 (55)	28 (53.8)	
*Previously surgery, n (%)	2 (10)	8 (15.4)	0.716
*Complaints, n (%)			
Abdominal pain	18 (90)	50 (96.2)	0.307
Nausea and / or vomiting	16 (80)	48 (92.3)	0.206
High temperature	3 (15)	7 (13.5)	0.567
Sensitivity in the right lower quadrant	15 (75)	47 (90.4)	0.228
Post operative local complications, n (%)	10 (50)	5 (9.6)	0.001
Laboratory, median (IQR 25–75)			
Hemoglobin (g/dL)	13.9 (12.07–15.1)	13.4 (12.5–14.5)	0.580
White blood cell ( $10^3/\mu\text{L}$ )	17.6 (13.4–20.5)	12.9 (9.5–15.3)	0.003
Neutrophil ( $10^3/\mu\text{L}$ )	15 (12.6–16.5)	10.2 (7.6–12.3)	0.001
Lymphocytes ( $10^3/\mu\text{L}$ )	1.2 (0.6–1.4)	1.6 (1.1–2.24)	0.012
Platelet ( $10^3/\mu\text{L}$ )	230 (186–286)	235 (192–290)	0.787
International normalized ratio	1.34 (1.10–1.72)	1.31 (1.09–1.68)	0.214
Glucose (mg/dL)	1.2 (1.1–1.34)	1.16 (1.05–1.25)	0.770
Blood urea nitrogen (mg/dL)	19 (15.2–30)	15.5 (13–20)	0.025
Creatinine (mg/dL)	1.1 (0.89–1.47)	0.9 (0.75–1.2)	0.038
Albumin (g/dL)	3.08 (2.5–3.4)	3.7 (3–4.2)	0.004
Total bilirubin (mg/dL)	1.2 (0.87–1.80)	0.96 (0.63–1.3)	0.041
Hospital stay duration, (days) median (IQR 25–75)	6 (4.2–9.2)	4 (3–6)	0.057
Time to surgery from pain starting, (hours) median (IQR 25–75)	14.5 (13–16.7)	13.2 (12–17)	0.096

**Table 3.** Multivariate regression model to predict in perforation

	p-value	Odds Ratio	95% CIs
Age	0.107	1.10	0.98–1.23
Gender	0.016	10	1.52–65.49
Time to surgery from pain starting	0.305	1.01	0.98–1.04
Neutrophil	0.012	1.25	1.05–1.50
Creatinine	0.90	0.86	0.92–8.13
Total bilirubin	0.492	1.26	0.65–2.43

countries. In Turkey, it has been shown that traditionally older men get hospitalized at later stages. In the literature, no relationship has been shown between common comorbid conditions in the elderly and the perforation of appendicitis.<sup>[12]</sup> However, in our study, we found that the perforation rate was higher in patients with CKD. CKD makes it more challenging to diagnose acute appendicitis in patients. CKD patients often have more comorbidities, and the risk of perforation increases, especially in dialysis treated CKD because of motor and endocrine dysfunctions of the gastrointestinal tract, poor abdominal examination findings, lack of fever response, and atypical laboratory results.<sup>[14–16]</sup>

The ability of the immune system to fight infections decreases with age in geriatric patients. Although the T-cell and leukocyte count do not decrease significantly with age, their functionality decreases, especially their ability to respond to new antigens.<sup>[9]</sup> Inflammatory markers of appendicitis in geriatric patients may vary depending on various factors, such as bone marrow capacity, liver synthesis function, comorbidities, and drugs. When inflammatory markers in patients were evaluated in the literature, the findings varied.<sup>[5,8,17,18]</sup> Neutrophilia with shift to the left is often associated with lymphopenia and may present with monocytosis, which is characteristic of an acute infection.<sup>[17,19]</sup> In the study by Markar et al.,<sup>[18]</sup> it was suggested that lymphopenia associated with clinical history may have a higher accuracy than C-reactive protein or leukocyte count in the diagnosis of acute appendicitis. In our results, lymphopenia was more evident in patients with perforated appendicitis. Yang et al.<sup>[19]</sup> analyzed the leukocyte count and percentage of neutrophils in a study of elderly patients as predictors of acute appendicitis versus another diagnosis, and found neither to be predictive of diagnosis. In the study by Sheu et al.,<sup>[8]</sup> rather than the neutrophil count, the left shift of leukocytes (band and seg >76%) was associated with a 2.24-fold risk of perforated appendicitis. Based on our results, the neutrophil count was also an independent predictor of perforated appendicitis. In the literature, there were reports that complications more frequent in the perforated groups compared to the non-perforated groups in the geriatric patients.<sup>[7,20]</sup> Sirikurnpiboon demonstrated a higher number of complications in perforated appendicitis.<sup>[7]</sup> Similarly, we found more local complications in perforated group.

Appendicitis in elderly patients is associated with increased risk of post-operative complications. The choice between laparoscopy and open appendectomy remains controversial in treating elderly patients with appendicitis. Our surgeons use laparoscopic method in geriatric patients. The use of laparoscopy in the elderly has increased significantly in recent years.<sup>[21]</sup> In general, the safety and efficacy of laparoscopic appendectomy are demonstrated by a reduction in mortality, complications, and hospital stay compared with open appendectomy. Harrell shows that laparoscopic approach to perforated appendix in elderly patients has advantages over open appendectomy in terms of reduced hospital stay and higher home discharge rate compared to rehabilitation centers, nursing homes, or skilled nursing care.<sup>[11]</sup> In a meta-analysis comparing laparoscopy with open appendectomy, it demonstrated that laparoscopic appendectomy is a safe and feasible procedure for elderly appendicitis patients with lower postoperative mortality and complication rates and shorter hospital stay.<sup>[21]</sup>

### Limitations

Our study has certain limitations. First, as a single-center study, our results cannot be generalized to other centers. For example, a rural institution may have a higher appendiceal

perforation rate than an urban institution where travel times to the emergency room are shorter. Second, because of the retrospective nature of the study, incomplete and erroneous data in the hospital records may have affected the results of the study. The low number of patients is another limitation of the study.

### Conclusion

In elderly patients who admit to the emergency department with abdominal pain, abdominal examination may be confusing and inadequate to make a diagnosis. Establishing a diagnosis of acute appendicitis in geriatric patients and consult these patients to surgery for definitive treatment in the shortest period is very important, especially for the emergency doctor. Failure to diagnose appendicitis at emergency service is related to an increased rate of perforation. In conclusion, based on the results of the present study, there is a greater risk of perforated appendicitis because of poor abdominal physical examination results in patients with comorbid CKD. In addition, male sex and a high neutrophil count were independent predictors of perforation.

**Ethics Committee Approval:** This study was approved by the Ankara Kecioren Training and Research Hospital Clinical Research Ethics Committee (Approval number: 2012-KAEK-15/2110, date: 10.06.2020).

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**Conflict of Interest:** None declared.

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## ORJİNAL ÇALIŞMA - ÖZ

### Geriatrik akut apandisitli hastalarda perforasyonla ilişkili faktörlerin belirlenmesi

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**AMAÇ:** Geriatrik hastalarda abdominal acillerinin tanınması ve tedavisi, genç popülasyona göre daha karmaşıktır. Biz bu çalışmada, akut apandisit tanısı alan geriatrik hastaların demografik özellikleri ve erken dönemde perforasyonla ilişkili faktörleri araştırmayı amaçladık.

**GEREÇ VE YÖNTEM:** Lokal etik kurul onayı alındıktan sonra, Ocak 2015–Aralık 2019 tarihleri arasında apandektomi yapılan 65 yaş ve üzeri hastalar çalışmaya alındı. Hastaların demografik verileri, fizik muayene bulguları, laboratuvar sonuçları incelendi. Hastalar, cerrahi raporlarına göre perfore ve basit apandisit olarak iki gruba ayrıldı.

**BULGULAR:** Çalışma süresince 72 hasta değerlendirildi. Çalışmamızda hastaların %48.6'sı erkek, ortanca yaş 71.5 idi (IQR 25–75, 68–80). Hastaların %28'inde perfore apandisit saptandı. Perfore apandisitli hastaların büyük çoğunluğunun erkek olduğu; kronik böbrek hastalığı ve ameliyat sonrası lokal komplikasyonların daha sık olduğu; lökosit, nötrofil, kan üre azotu, kreatinin ve toplam bilirubin değerlerinin yüksek; albümin değerlerinin daha düşük olduğunu tespit ettik ve bu farklılıklar istatistiksel olarak anlamlıydı (tüm değerler,  $p < 0.05$ ). Çok değişkenli analiz ise artmış nötrofil sayısının ve erkek cinsiyetin perfore apandisit ile anlamlı olarak ilişkili olduğunu gösterdi (sırasıyla,  $p = 0.035$ ,  $p = 0.01$ ).

**TARTIŞMA:** Kronik böbrek hastalığı olan geriatrik hastalarda yetersiz kanın fizik muayene sonuçları nedeniyle perforasyon apandisit riski daha fazladır. Ek olarak, erkek cinsiyet ve artmış nötrofil sayısı perforasyonun bağımsız belirleyicileridir.

**Anahtar sözcükler:** Akut apandisit; geriatrik; perforasyon.

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