How Can We Manage the Therapeutic Approach of Acute Diverticulitis Regarding the Number of Attacks?

Akut Divertikülit Tedavisi; Atak Sayısına Göre Yaklaşım Nasıl Olmalıdır?

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ABSTRACT

Aim: The risk of acute diverticulitis (AD) increases with each attack and the decision of therapeutic management is getting more complicated. We aimed to investigate the effective features of the number of attacks.

Method: Two hundred thirty six patients with AD defined by computerized tomography were retrospectively analyzed according to the number of attacks $(1, 2, and \geq 3)$.

Results: 45.8% patients were female. The mean age was 58.3±12.7 years old, mean body mass index was 28.8±6.5 kg/m². Elective colonoscopy of AD was mostly localized in the left colon (p<0.05). The majority of the patients had a conservative treatment regardless of several attacks (81.4%). The percentage of patients received a conservative treatment (83.6% vs 81.1% and 75.5%) and radiological abscess drainage (10.5% vs 5.7% vs 6.1%) were higher in the patients with first attack (p=0.012). The percentage of patients undergone abscess drainage by open surgery (0.7% vs, 5.7% vs 12.2%) was higher in the patients with \geq 3 attacks, while the number of segmental colon resection (7.5% vs 61% vs 5.2%) was higher in the patients with 2 attacks (p=0.012). The increase in Hinchey classification had an impact on the invasive interventions regarding the clinical parameters of AD [odds ratio (OR): 0.052; 95% confidence interval (CI): 0.022-0.126; p<0.001]. The patients with older age were more likely to be treated with surgical interventions (OR: 0.960; 95% CI: 0.918-1.003; p=0.07).

Conclusion: The increases in Hinchey classification with older age has a potential impact among the invasive abscess drainage and surgical intervention regarding the severity of each attack of AD.

Keywords: Abdominal abscesses, acute diverticulitis, colonoscopy

ÖZ I

Amaç: Akut divertikülit (AD) riski her atakta artmakta ve tedavi yönteminin kararı daha karmaşık hale gelebilmektedir. Çalışmamızda atak sayısını etkileyen faktörleri araştırmayı amaçladık.

Yöntem: Bilgisayarlı tomografi ile tanımlanmış 236 AD hastası retrospektif olarak atak sayısına (1, 2 ve ≥3) göre değerlendirildi.

Bulgular: Hastaların %45,8'i kadındı. Ortalama yaş 58,3±12,7, ortalama vücut kitle indeksi 28,8±6,5 kg/m² idi. Yapılan elektif kolonoskopilerde hastalık, çoğunlukla solda (sol kolon %60,2 ile sağ kolon %10,6) solda lokalize idi. Hastaların büyük bir kısmına, atak sayısından bağımsız olarak konservatif tedavi (%81,4) verildi. Hastalara ilk ataklarında %83,6 oranında konservatif tedavi ve %10,5 oranında radyolojik apse drenajı uygulandı (p=0,012). Üç ve daha fazla atak geçirenlerde sıklıkla açık cerrahi ile apse drenajı yapıldı (%12,2). İki atak geçiren hastalarda ise segmental kolon rezeksiyonu sayısı (%7,5) daha yüksek oranda izlendi (p=0,012). Hinchey sınıflamasına göre evre, AD tedavisinde invaziv yöntemlerin kullanılmasında anlamlı derecede etkilidir [odds ratio (OR): 0,052; %95 güven aralığı (GA): 0,022-0,126; p<0,001]. İleri yaşlarda hastalara daha çok cerrahi tedavi uygulanmıştır (OR: 0,960; %95 CI: 0,918-1,003; p=0,07).

Sonuç: Hinchey sınıflamasına göre ileri evre ve yaşla birlikte, geçirilen AD atağının şiddetine bağlı olarak hastalarda cerrahi apse drenajı veya cerrahi müdahale ihtiyacında potansiyel bir artış izlenmiştir.

Anahtar Kelimeler: Abdominal apse, kolonik divertikülit, kolonoskopi



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Introduction

Acute diverticulitis (AD) is a serious inflammatory disease that occurs in 25% of patients with diverticulosis, involving the colon. AD is frequently encountered in the emergency room of general surgery due to the severity of its consequences. Up to 20% of patients hospitalised for AD need surgery for septic, haemorrhagic and/or obstructive complications.¹ The diagnosis of AD is performed by a clinical examination and abdominal tomography. In general, AD occurs in attacks, and its characterisation is based on the patient's presentation at the time of the initial attack of AD and on the appearance of disease on computerised tomography imaging during the initial visit.^{2,3,4}

Approximately 10% of patients with diverticulitis develop complications, such as an abscess or free perforation, which require close observation and further treatment with antibiotics, percutaneous drainage or open surgery.^{2,5} The risk of complications increases with each attack of AD. As a result of radiological imaging performed in each attack or during follow-up, the choice of conservative or elective or surgical intervention is made according to the Hinchey stage, a widely used classification of the degree of intraperitoneal contamination.^{6,7} Elective surgery is generally delayed at least 6 weeks after the first episode so that the inflammation and infection resolve considerably. Unfortunately, emergency surgery cannot be postponed in some situations, and in these cases, the magnitude of intraperitoneal contamination dictates the choice of reconstruction. Generally, with localised contamination, observed in grades I and II, a primary anastomosis without a protective ostomy can be performed, while with more diffuse contamination, observed in grades III and IV, a twostage procedure is generally preferred; either a Hartmann's procedure or a primary anastomosis with a protective proximal diverting stoma.8

Recurrent diverticulitis can occur in 20%-35% of patients after a first acute attack of AD treated non-surgically.⁹ Rarely, it can also present in patients after resection for sigmoid diverticulitis despite complete remission. Moreover, 36% of people have ongoing abdominal symptoms after the first episode of diverticulitis.¹⁰ As the incidence of diverticulitis increases, the risk of recurrent attacks is expected to increase with each attack. There is insufficient literature to determine the management of AD in each admission of a patient who has never undergone surgical intervention for AD before the primary attack. Historically, surgery was advised after two attacks of AD and after the first attack in patients younger than 40 years.¹¹ This has been challenged recently by a new approach to individualise treatment depending on the rates of previous AD events and frequency of attacks as well as the patient's immune status and the presence of complications such as chronic pain.^{4,8} In this study, we aimed to investigate the effect of the number of attacks on the follow-up of patients with a surgical or conservative approach, as well as the decision to perform emergency surgery in AD cases.

Materials and Methods

The study protocol was approved by the Clinical Research Ethics Committee of the Bağcılar Training and Research Hospital of Health Science University (no: 2020.01.2.02.012). All procedures performed in this study involving human participants followed the ethical standards of the institutional research committee and the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Study Population

Patients (236) who applied to University of Health Sciences Turkey, Bağcılar Training and Research Hospital between June 2016 and January 2020 and were diagnosed with AD according to a clinical examination, radiological imaging and elective colonoscopy were included in the study and analysed retrospectively. The medical records were evaluated. All readmissions to the emergency unit and medical care received after discharge at our facility were captured to documents. Patients older than 18 years who underwent elective colonoscopy for a primary diagnosis of diverticulitis were included in the final analysis and divided into three groups according to the number of diverticulitis attacks as Attack 1 (applied for only 1 attack), Attack 2 (applied for 2 attacks) and Attack \geq 3 (applied for 3 or more attacks). Patients younger than 18 years and those who underwent colectomy with a diagnosis of colon or rectal cancer or inflammatory bowel diseases or benign diseases were excluded from the study. We performed a colonoscopy during the follow-up period on patients who had been previously diagnosed with diverticulitis clinically and radiologically. If the patient had a colonoscopy without an accurate diagnosis of diverticulitis, it was excluded.

Variables and Outcomes

The demographic, radiological and per-operative clinical findings and haematological parameters at admission were recorded and categorised retrospectively. Demographic characteristics included age, sex, body mass index (BMI, kg/m²), smoking and alcohol usage status, comorbidities [hypertension, diabetes mellitus, chronic obstructive pulmonary disease (COPD)], functional health status and history of colorectal cancer (CRC). Clinical outcomes were Hinchey classification, laboratory parameters, localisation of diverticulitis according to CT imaging and colonoscopy and treatment management, namely either by conservative

treatment or by abscess drainage or by segmental colon resection such as the Hartman procedure. We did not include any elective surgery, which was very limited in our clinic. We evaluated radiological or surgical drainage and segmental colon resection at the onset of emergency settings following their clinical assessments and examinations regarding their emergency admissions.

Clinically, diverticulitis was separated into complicated and uncomplicated disease, based on the Hinchey system.⁴ Among the laboratory parameters routinely measured during admission, only white blood cell count (WBC), haematocrit (HTC) and albumin (ALB) concentration were analysed. The reference ranges of WBC, HTC and ALB levels were 3.8-10.8x103/µL, 35%-50% and 3.4-5.4 g/dL, respectively.

Statistical Analysis

Descriptive statistics were reported as percentages for categorical variables and as means with standard deviations for continuous variables. The normality of the distribution of variables was examined by using the Kolmogorov-Smirnov test. The comparisons of the variables between groups were performed either by one-way ANOVA or by the Kruskal-Wallis test (non-parametric ANOVA). Univariate analysis comparing patients according to selective therapeutic management of AD cases were performed using the chi-square test for categorical variables and the t-test for continuous variables. Multivariate analyses with logistic regression were performed to identify the impact of risk factors on invasive therapeutic management to control potential confounders. p<0.05 was considered to indicate statistical significance. The analysis was performed with IBM SPSS Statistics, Version 23 (Armonk, NY: IBM Corp.).

Results

Of the 236 patients diagnosed with AD, 108 (45.8%) were female and 128 (54.2%) were male. The mean age of all patients was 58.3 ± 12.7 years, and the mean BMI was 28.8 ± 6.5 . It was determined that the mean age, sex distribution, number of patients with COPD or hypertension, CRC history, rate of alcohol usage and smoking status did not differ among patients according to the number of attacks (Table 1). On the other hand, patients with 2 attacks were more likely to have a higher BMI (28.7 ± 5.8 vs 30.3 ± 9.0 vs 27.3 ± 4.3 , p=0.08). In addition, patients who had 3 or more attacks showed a significantly higher incidence of DM disease (1.5% vs.7.5% vs. 10.2% p=0.03).

According to the patients' functional health status, the majority of patients (88.1%) were functionally independent (Table 1). However, the percentage of partially dependent

Characteristics	Total (n=236)	Attack 1 (n=134)	Attack 2 (n=53)	Attack ≥3 (n=49)	p value
Age (X ± SD) (min-max)	58.3±12.7 [27-89]	58.4±12.7 [27-89]	57.6±13.5 [32-85]	58.5±11.8 [34-81]	0.92
Sex n (%) Male Female	128 (54.2) 108 (45.8)	76 (56.7) 58 (43.3)	29 (54.7) 24 (45.3)	23 (46.9) 26 (53.1)	0.50
BMI (X ± SD) (min-max)	28.8±6.5 [18.2-82.2]	28.7±5.8 [18.4-43.6]	30.3±9.0 [18.2-82.2]	27.3±4.3 [19.4-43.6]	0.08
Comorbidities, n (%) DM COPD Hypertension	11 (4.7) 16 (6.8) 74 (31.4)	2 (1.5) 9 (6.7) 45 (33.6)	4 (7.5) 5 (9.4) 18 (33.96)	5 (10.2) 2 (4.1) 11 (22.5)	0.03 0.56 0.32
Functional health status, n (%) Independent Partially dependent Totally dependent	208 (88.1) 19 (8.1) 9 (3.8)	121 (90.3) 6 (4.5) 7 (5.2)	42 (79.2) 10 (18.9) 1 (1.9)	45 (91.8) 3 (6.1) 1 (2.0)	0.02
Alcohol usage, n (%)	6 (2.5)	2 (1.5)	3 (5.7)	1 (2.0)	0.26
Smoking, n (%) CRC history, n (%)	33 (14.0) 8 (3.4)	20 (14.9) 5 (3.7)	8 (15.1) 1 (1.9)	5 (10.2) 2 (4.1)	0.69 0.79

Table 1. Demographic characteristics of patients compared with the number of attacks of acute diverticulitis

X ± SD: Mean ± standard deviation, DM: Diabetes mellitus, COPD: Chronic obstructive pulmonary disease, CRC: Colorectal cancer, min: Minimum, max: Maximum

patients was significantly higher in patients with 2 attacks (4.5% vs 18.9% vs 6.1%) while the percentage of totally dependent patients was considerably higher in patients with one attack (5.2% vs 1.9% vs 2.0%, p=0.02) (Table 1).

The evaluated clinical characteristics of patients, such as WBC, HTC and ALB; localisation of diverticulitis and Hinchey stage did not differ statistically with respect to the number of AD attacks (Table 2). However, clinically, simple AD (Hinchey stage 0 and I) was observed mostly in patients with one attack (19.4% and 44.0%, respectively) and two attacks (18.9% and 49.1%, respectively) (p=0.49). Patients with \geq 3 attacks were more likely to be diagnosed with complicated AD, which was correlated with the higher stages of the Hinchey classification (Hinchey II, III and IV), (26.5%, 10.2% and 10.2%, respectively) (p=0.49). Moreover, elective colonoscopy examination showed AD mostly localised in the left colon and less frequently in bilateral localisation (60.2% vs 7.2%, p=0.006). The percentage of patients who had a first attack also had AD mostly in the left colon (61.9% vs 54.7% vs 61.2%, p=0.006) (Table 2).

Comparing treatment management, the majority of patients received a conservative treatment (81.4%) regardless of the number of attacks (Table 2). The percentage of patients who received conservative treatment (83.6% vs 81.1% vs 75.5%, respectively) and radiological percutaneous abscess drainage (10.5% vs 5.7% vs 6.1%, respectively) was significantly higher in patients with a first attack (p=0.012).

Segmental colon resection such as the Hartman procedure was a less likely option in the first attack (5.2% vs 7.5% and 6.1%, p=0.012). Percutaneous abscess drainage was performed more than open surgical drainage in patients with one attack (10.5% vs 0.7%, p=0.012). The percentage of patients who underwent abscess drainage by open surgery (0.7% vs 5.7% vs 12.2%) was highest in patients with \geq 3 attacks, while the percentage of segmental colon resection (5.2% and 7.5% vs 6.1%) was higher in patients with 2 attacks, respectively (p=0.012) (Table 2).

Univariate regression analysis of all variables showed that older age [odds ratio (OR): 1.038; 95% confidence interval (CI): 1.009-1.068; p=0.01] and increased Hinchey stage of

	Total (n=236)	Attack 1 (n=134)	Attack 2 (n=53)	Attack \ge 3 (n=49)	p value
Laboratory data WBC	X ± SD 8.3±3.5	8.3±3.5	8.6±3.2	8.4±3.9	0.46
HTC ALB	39.5±5.4 3.72±0.7	39.9±5.4 3.7±0.7	38.5±5.4 3.6 0.7	39.5±5.5 3.8±0.7	0.26 0.21
CT localization, n (%) Right Left Bilateral	36 (15.3) 183 (77.5) 17 (7.2)	14 (19.5) 111 (82.8) 9 (6.7)	10 (18.9) 37 (69.8) 6 (11.3)	12 (24.5) 35 (71.4) 2 (4.1)	0.08
Hinchey stage, n (%) 0 I II III IV	44 (18.6) 103 (43.6) 49 (20.8) 29 (12.3) 11 (4.7)	26 (19.4) 59 (44.0) 25 (18.7) 19 (14.2) 5 (3.7)	10 (18.9) 26 (49.1) 11 (20.8) 5 (9.4) 1 (1.9)	8 (16.3) 18 (36.7) 13 (26.5) 5 (10.2) 5 (10.2)	0.49
Colonoscopic localization, n (%) None Right Left Bilateral	52 (22.0) 25 (10.6) 142 (60.2) 17 (7.2)	30 (22.4) 10 (7.5) 83 (61.9) 11 (8.2)	17 (32.1) 3 (5.7) 29 (54.7) 4 (7.5)	5 (10.2) 12 (24.5) 30 (61.2) 2 (4.1)	0.006
Management, n (%) Conservative treatment Percutaneous abscess drainage Abscess drainage by open surgery Segmental colon resection	192(81.4) 20 (8.5) 10 (4.2) 14 (5.9)	112 (83.6) 14 (10.5) 1 (0.7) 7 (5.2)	43 (81.1) 3 (5.7) 3 (5.7) 4 (7.5)	37 (75.5) 3 (6.1) 6 (12.2) 3 (6.1)	0.012

Table 2. Clinical characteristics and intraoperative findings of patients compared with the number of attacks of acute diverticulitis

X ± SD: Mean ± standard deviation, CT: Computerized tomography, WBC: White blood cell, HTC: Hematocrit, ALB: Albumin

AD (OR: 19.65; 95% CI: 8.212-47.01; p<0.001) primarily affected the surgical therapeutic approach (Table 3). However, other demographic characteristics and clinical parameters did not affect the therapeutic approach, regardless of the increase in the number of attacks (Table 3). The increase in Hinchey classification had an impact on invasive interventions with respect to clinical parameters of AD (OR: 0.052; 95% CI: 0.022-0.126; p<0.001) (Table 4). Multivariate analysis adjusted for age showed that older patients were more likely to be treated with surgical intervention (OR: 0.960; 95% CI: 0.918-1.003; p=0.07).

Discussion

Various attack numbers, which have an impact on the progress of AD, have been reported in 10%–25% of diverticulitis patients.¹² The role of prophylactic surgery following conservatively treated AD is controversial in

numerous studies.^{12,13,14} Prevention of recurrent acute attacks and the need for urgent surgery are some of the important inconveniences with the assessment of AD during elective follow-up.¹⁵ In this single-centre, retrospective study, we focused on the attack number in patients with AD and its effect on clinical outcomes and decision making regarding conservative management of the disease.

In previous studies based on identification of predictors of persistent, complicated diverticular disease, it was found that the number of attacks did not increase the patient's risk of persistent complexity.⁴ However, Nizri et al.¹⁶ reported that the first attack of complicated diverticulitis was the main risk factor associated with eventual complications compared with the number of recurrent attacks. In contrast, Van de Wall et al.¹⁰ reported that a major effect of previous attacks of diverticulitis since patients with uncomplicated diverticulitis had a higher number of previous attacks than

Table 3. Unadjusted	covariates for the management	of the acute diverticulitis

DM: Diabetes Mellitus, COPD: Chronic obstructive pulmonary disease, CRC: Colorectal cancer, CT: Computerized tomography, WBC: White blood cell, HTC: Hematocrit, ALB: Albumin, BMI: Body mass index, CI: Confidence interval

Table 4. Adjusted	covariates for	the management	of the acute	diverticulitis

Management of treatment	Odds ratio	95% CI	p value
Hinchey	0.052	0.022-0.126	<0.001
Age	0.960	0.918-1.003	0.07

CI: Confidence interval

patients with complicated diverticulitis. In the present study, an increasing number of attacks were detected in higher stages of the Hinchey classification, considering that AD could be more complicated in Hinchey II, III and IV.

Considering the variable factors in AD, some studies underscored the fact that patients presenting with complicated diverticulitis frequently have a more complex clinical presentation. Many of these factors have been studied from different clinical perspectives.^{4,9,17,18,19,20,21} Patients prone to comorbidities may also carry an increased risk of AD due to the pathophysiology of diseases such as diabetes mellitus. Moreover, ageing, alcohol use, obesity and smoking may also enhance both the immune system and the tissue-healing pathways of the intestinal system.^{17,18,19,20,21,22} In some previous studies, it was reported that complicated diverticulitis was more likely to present with a lower functional status and be associated with increasing age and alcohol use.⁴

Consistently in our study, the number of patients with diabetes mellitus was significantly higher in patients with \geq 3 attacks. According to functional health status, the percentage of partial dependence was significantly higher among patients with 2 attacks. This may be related to the limited number of patients included in the analysis, based on the data and the observational study. Still, our findings suggest that the risk for AD may increase with the increasing number of attacks regarding the severity of attacks, especially in patients with a lower functional status.

Today, the indications for emergency surgery in the management of AD at the first attack of the disease are becoming more controversial. For AD cases, an optional sigmoid colectomy has only been suggested following the urgent Hinchey evaluation and the clinical view on the individual patient's condition such as age, functional health status, number and severity of attacks and severity of symptoms.¹¹ However, there are some reports stating that elective surgery is indicated more frequently in patients with recurrent attacks and the presence of persistent symptoms.¹⁵ This statement may have been affected by various reported clinical parameters about an elective resection after two attacks of AD.23 In our study comparing the surgical and conservative management of treatment, the majority of patients received conservative treatment regardless of the number of attacks. Moreover, segmental colon resection such as the Hartman procedure was less likely to be an option at the first attack. Percutaneous abscess drainage with radiological intervention was performed more often in patients with one attack than abscess drainage with open surgery. Open surgical drainage was mostly performed in patients who had \geq 3 attacks, suggesting that each attack might cause a change among individual patterns of disease severity.

An early focus on the diagnosis of diverticulitis might give a clue to designing a successful treatment algorithm according to the degree of disease and other demographic parameters. To support disease management, CT evaluations, hospitalisation at the time of the first attack, longer courses of antibiotic treatment and closer radiological imaging may be needed in follow-up.^{4,17,18,19,20,21} Moreover, if a patient presents with several factors that may increase the risk of complicated diverticulitis resulting in poor prognosis, a colonic resection may be indicated rather than after multiple percutaneous drainage procedures and longterm application of antibiotics.^{4,17,18,19,20,21} A primary crucial indication for surgery is the Hinchey classification.^{6,7} In our study, the Hinchey classification of each attack of AD was more likely to impact on invasive interventions regarding attack numbers and the clinical parameters of AD in our population. Suarez Alecha et al.¹⁵ evaluated the safety of conservative management and the risk factors for emergency surgery after the first episode of AD.¹⁵ They concluded that after an attack of AD, the nonoperative approach is safe because fewer number of patients, less than 5%, will need an emergent procedure in a subsequent attack of AD. They also add that the first attack of complicated AD can be a risk factor for emergency surgery in conservatively treated patients.15 The Hinchey classification should be considered to decide the need for urgent surgery or elective surgery following each attack of AD to decrease further attacks.8

The need for surgery after recovery from AD in patients younger than 50 years of age remains controversial.^{15,19,24} Some reports showed that ageing has no differences in attacks of AD compared to older patients regarding surgical procedures.^{15,24} Our regression analysis showed that aging patients were often treated with invasive radiological and surgical interventions regarding the complexity of AD and an increase in attacks.

Study Limitations

The limitations of our study are that a small number of patients were analysed retrospectively from the data from a single centre without comparison with elective cases and AD groups from a restricted region (Bağcılar area), which may limit generalisation to other regions and groups. Our study was limited by its retrospective nature, which may have induced measurement, observational and recall biases. Despite these limitations, this study is the first report that evaluated the predictive factors for urgent therapeutic management for AD in the Bağcılar region of Istanbul, suggesting a prediction model for the therapeutic management of AD at the time of diagnosis based on attack number.

Conclusion

In conclusion, an increase in the number of AD attacks should be considered during clinical follow-up regarding disease severity. Our prediction model might be a helpful clinical tool to select the proper therapeutic approach for the management of AD patients depending on the number of attacks. Treatment of AD should be patientoriented with special attention to the number of attacks and the severity of the disease. Invasive procedures must be chosen carefully, considering the risks of surgical intervention, to improve postoperative outcomes. The early recognition of complicated diverticulitis before urgent surgery and optional therapy based on disease progression in frail patients are warranted. Further multi-institutional, prospective, randomised control studies on a large sample size are needed to validate our model.

Ethics

Ethics Committee Approval: University of Health Sciences Turkey, Bağcılar Training and Research Hospital Clinical Research Ethics Committee (decision number: 2020.01.2.02.012)

Informed Consent: For this type of study formal consent is not required.

Peer-review: Externally and internally peer review.

Authorship Contributions

Surgical and Medical Practices: Y.A., N.A.H., S.M., Concept: Y.A., N.A.H., Design: Y.A., Data Collection or Processing: N.A.H., M.T., Analysis or Interpretation: S.M., A.A., Literature Search: N.A.H., M.T., Writing: Y.A., A..A.

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

Financial Disclosure: The authors declared that this study received no financial support.

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