

## Evaluation of follow-up colonoscopy in acute colonic diverticulitis for detection of advanced adenoma and colon cancer: a retrospective cohort study

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### Abstract

**Background:** Due to variable rates of colon carcinoma or advanced adenoma mimicking an acute diverticulitis episode, the necessity of colonoscopy to detect colon cancer or advanced adenoma remains to be explored. This study investigated the incidence and predictive factors of colon cancer or advanced adenoma following acute diverticulitis.

**Methods:** We evaluated retrospectively all consecutive patients with an episode of computed tomography-proven acute diverticulitis between June 2016 and August 2019. A follow-up colonoscopy was performed. Demographic and clinical parameters were recorded.

Patients with clinically substantial colonic neoplasia (colon cancer or advanced adenoma) were classified as Group A, while Group B included patients without clinically significant colonic neoplasia. The incidence of clinically significant colonic neoplasia in acute diverticulitis patients was regarded as the primary outcome.

**Results:** The mean age of 233 patients with acute diverticulitis was  $58.6 \pm 12.7$  years. Complicated diverticulitis was detected in 39 patients (16.7 %). Sixteen patients (6.9 %) were assigned to Group A and 217 patients (93.1 %) to Group B. The age of the patients in group A was significantly higher than in Group B ( $p = 0.001$ ). Age above 50 and 65 years was also significantly associated with clinically significant colonic neoplasia ( $p = 0.015$  and  $p = 0.012$ , respectively). The other variables did not influence the development of clinically significant colonic neoplasia ( $p > 0.05$ ).

**Conclusions:** Colonoscopy examination following an episode of acute diverticulitis may not be recommended for all patients due to the rare occurrence of colon cancer or clinically significant colonic neoplasia in those younger than 50 years. HIPPOKRATIA 2021, 25 (2):69-74.

**Keywords:** Acute diverticulitis, colonoscopy, colon cancer, adenoma

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### Introduction

The diverticular disease often occurs on the left side of the colon, specifically at the sigmoid colon, and is usually observed in the elderly in the western countries<sup>1,2</sup>. Diverticular disease's pathogenesis is thought to be multifactorial, including several environmental and genetic factors. Acute colonic diverticulitis (ACD) is an inflammatory process that complicates the condition with 10 to 25 % incidence rate. Besides, the risk of diverticulitis increases for each episode<sup>1</sup>.

Colon carcinoma mimicking ACD can be detected with an average incidence of 2.1 %, and the rates vary in uncomplicated and complicated diverticulitis<sup>3-5</sup>. Considering this low incidence of colon carcinoma in patients with ACD, routine colonoscopy after abdominal computed tomography (CT) is controversial. Besides being

invasive, colonoscopy is a time-consuming and costly procedure with potential risks of perforation and bleeding in those patients<sup>3,6,7</sup>. Furthermore, it has been speculated that there is no significant association between colon cancer risk and an episode of uncomplicated ACD. The risk or prevalence of clinically significant colonic neoplasia (CSCN), including colon cancer and advanced adenoma, is thought to be higher in patients with CT-proven acute diverticulitis<sup>8-10</sup>. Thus, the usefulness of colonoscopy on the detection of CSCN following an acute episode of ACD remains to be clarified.

Most previously published studies used a retrospective design considering the low incidence of colon cancer following ACD<sup>4,8-10</sup>, while in a limited number of studies, the incidence of colon cancer was prospectively investigated<sup>11-13</sup>. In those studies, the sample size was relatively

small (less than 150), and colon cancer detection was nil in two of them<sup>11,12</sup>. Considering these findings, we regard the retrospective design as advantageous in investigating the colon cancer incidence in patients with ACD.

In this study, we aimed to investigate the incidence of colon cancer, or CSCN diagnosed during the follow-up colonoscopy performed following an episode of CT-proven diverticulitis and evaluate the predictive factors for the development of colon cancer or CSCN in those patients.

## Materials and Methods

### Study

Medical records of the patients with ACD were retrospectively reviewed from June 2016 through August 2019 at Bagcilar Training and Research Hospital, Istanbul, Turkey. The onset of the study period was selected, taking into account the availability of the radiology and hospital information systems. All procedures performed in this study were in agreement with the Helsinki Declaration. The institutional Ethical Committee approved the study (decision No 2020.01.2.01.011). Due to the study's retrospective design, written informed consent was not required.

### Patients

The study included the patients admitted to the emergency department with a diagnosis of ACD. Patients were retrospectively identified through the radiology and hospital information systems by entering "acute diverticulitis" into a keyword search system. We also used the imaging methods (i.e., CT) and the study period (June 2016 to August 2019). The system automatically searched previously dictated CT reports during the designated periods with the words "acute diverticulosis". All CT scans were performed with intravenous contrast administration and evaluated by radiologists specialized in abdominal imaging for at least five years. We obtained relevant clinical data from the records of general surgery clinics and endoscopy units, and we reviewed all clinical and imaging reports to confirm whether they were consistent with ACD or not.

We included in the study all patients aged 18 years or older with an episode of CT-proven acute diverticulitis. We omitted patients with a prior endoscopic polypectomy and a complete colonoscopy the two years preceding the index admission. We evaluated the first colonoscopy report during or after the index admission or CT's statement closest to the colonoscopy in multiple admissions. ACD was diagnosed in the presence of a colonic diverticulum, pericolic inflammation, wall thickening of the colon greater than 3 mm on the lumen's short axis, and pericolic fat stranding in association with or without abscess formation or contained or free extraluminal air on

CT scans. We classified the severity of the diverticulosis using the modified Hinchey Classification by Wasvary<sup>14-16</sup>. We determined patients as uncomplicated ACD if the modified Hinchey score was 0 to 1b and as complicated ACD if the modified Hinchey score was 2 to 4.

All patients were hospitalized and initially administered medical treatment with parenteral broad-spectrum antibiotics (ceftriaxone 2000 mg/day and metronidazole 1500 mg/day). In case of failure of the medical treatment, percutaneous/surgical drainage or emergent surgical treatment were decided at the consultant surgeons' discretion. A follow-up colonoscopy was recommended 6-8 weeks after the discharge. We did not perform an endoscopic evaluation before surgery in patients with emergent surgical treatment.

### Variables

Demographic (age and sex) and clinical variables, including the number of previous ACD attacks, history of familial colorectal cancer, CT findings classified according to the modified Hinchey score, interval from CT to colonoscopy, colonoscopic findings, and histopathological diagnoses were recorded. As in previous studies, the patients' age was analyzed as <50 and ≥50 years, and <65 and ≥65 years<sup>17-19</sup>. The number of prior attacks was grouped as one attack and more than one attack. The colon's diverticular disease was classified as left-sided (distal to splenic flexure), right-sided (from cecum to transverse colon), and bilateral/diffuse, depending on the detection of the diverticula on colonoscopy. Advanced adenoma was defined as an adenoma with a villous component >25 %, high-grade dysplasia, or polyp sized >1 cm<sup>10,20,21</sup>. The presence of advanced adenoma or histopathologically proven colon cancer was regarded as CSCN. Group A included those patients with advanced adenoma or histopathologically proven colon cancer, while patients with ACD without CSCN were considered Group B.

### Statistical analysis

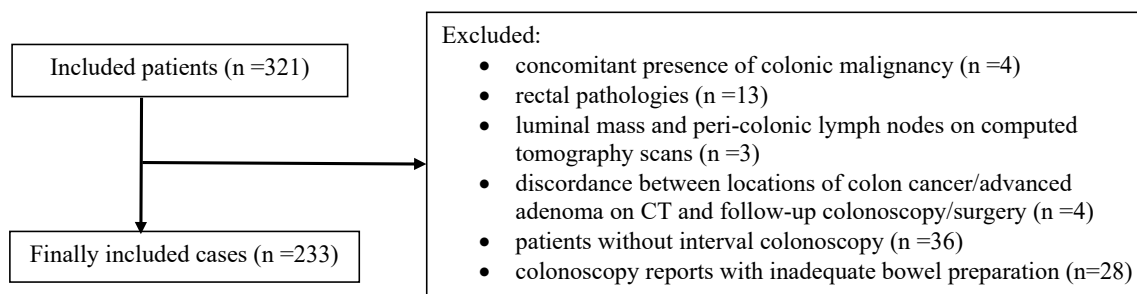
We performed statistical analysis using the statistical package SPSS for Windows, Version 15.0 (SPSS Inc., Chicago, IL, USA). The incidence of CSCN (advanced adenoma or colon carcinoma) in patients with ACD was the primary outcome. The normality of data distribution was assessed utilizing the Kolmogorov-Smirnov test in continuous variables. Continuous variables with normal distribution are presented as means with standard deviations, while those without as medians with interquartile range (IQR). Categorical variables are expressed as frequencies and percentages. The t-test, the  $\chi^2$  test, or Fisher exact test were used for the descriptive statistical analysis. Statistical significance was defined as  $p < 0.05$ .

## Results

In the retrospective search, 321 patients were identified with an ACD diagnosis. After excluding 88 cases (Figure 1), a total of 233 patients with a mean age of  $58.6 \pm 12.7$  years were finally included in the study. One hundred twenty-five patients were male (53.6 %). The median number of previous attacks was one [IQR (1-2)]. In 133 patients (57.1 %), the ACD attack was the first, while 100 patients (42.9 %) had more than one attack. Regarding location, left-sided colonic diverticular disease was more common (78.1 %) than right-sided (14.6 %) or bilateral/diffuse colonic diverticulitis (7.3 %).

In the study group, Hinchey type Ia ACD (102 patients, 43.8 %) was the most commonly seen ACD type. Complicated diverticulitis was detected in 39 patients (16.7 %). Demographic, clinical, and imaging features are given in Table 1.

The study group required sixteen percutaneous and ten surgical drainages of intraabdominal abscesses. Besides those, emergent segmental resection of the involved colon was performed in 11 patients (sigmoid resection/left hemicolectomy in ten patients and right hemicolectomy in one patient). Post ACD attack colonoscopy was



**Figure 1:** Flowchart of patient's selection in the current study that evaluated retrospectively all consecutive patients with an episode of computed tomography-proven acute diverticulitis between June 2016 and August 2019.

**Table 1:** Demographic and clinical features of the 233 acute diverticulitis patients included in the study.

Variable		Overall (n =233)	Group A (n =16)	Group B (n =217)	P
Age (year) *		$58.6 \pm 12.7$	$68.1 \pm 8.4$	$57.9 \pm 12.7$	0.001
Age groups †	<50 years	55 (23.6)	0 (0)	55 (25.3)	0.015
	≥ 50 years	178 (76.4)	16 (100)	162 (74.7)	
Age groups †	<65 years	157 (67.4)	6 (37.5)	151 (69.6)	0.012
	≥ 65 years	76 (32.6)	10 (62.5)	66 (30.4)	
Sex †	Female	108 (46.4)	9 (56.2)	99 (45.6)	0.446
	Male	125 (53.6)	7 (43.8)	118 (54.4)	
Number of attacks ‡		1 (1-2)	2 (1-2)	1 (1-2)	0.728
Attack groups †	1	133 (57.1)	8 (50.0)	92 (42.4)	0.607
	≥2	100 (42.9)	8 (50.0)	125 (57.6)	
Presence of CRC family history †		9 (3.9)	1	8	0.479
Localization of diverticula †	Right-sided	34 (14.6)	0 (0)	34 (15.7)	0.209
	Left-sided	182 (78.1)	15 (93.8)	167 (77.0)	
	Bilateral	17 (7.3)	1 (6.2)	16 (7.4)	
Hinchey classification †	0	44 (18.9)	2 (12.5)	42 (19.4)	0.094
	1a	102 (43.8)	3 (18.8)	99 (45.6)	
	1b	48 (20.6)	9 (56.2)	39 (18.0)	
	2	30 (12.9)	2 (12.5)	28 (12.9)	
	3	9 (3.9)	0 (0)	9 (4.1)	
	4	0 (0)	0 (0)	0 (0)	
Diverticulitis groups †	Uncomplicated	194 (83.7)	14 (87.5)	180 (83)	1.0
	Complicated	39 (16.7)	2 (12.5)	37 (17)	
Interval for colonoscopy (months) ‡		5 (4-8)	5 (4-6)	6 (4-9)	0.216

Values are presented as \*: mean  $\pm$  standard deviation, †: number with percentage in brackets, or ‡: median with interquartile range in brackets.

**Table 2:** Colonoscopic and histopathology findings of the 233 acute diverticulitis patients included in the study.

Pathology	Localization/pathology	Number of patients
Colon cancer (n =8)	Sigmoid colon	6
	Descending colon	1
	Ascending colon	1
Advanced adenoma (n =8)*	High-grade dysplasia	5
	>25 % villous component	7
	>1 cm in size	5
Adenoma-polyp	Moderate dysplasia	2
	Mild dysplasia	11
	Hyperplastic polyps	10
Inflammatory bowel disease		5
Leiomyoma		1

\*: Each polyp may contain more than one feature.

performed during an interval of five months median period [IQR (four to eight months)]. Diverticular disease was detected in colonoscopy in 189 patients (81.1 %). The findings of the colonoscopy screenings are summarized in Table 2. Eight patients (3.4 %) had biopsy-proven colon adenocarcinoma and eight patients (3.4 %) had advanced adenoma. The CSCN rate was 6.9 % (16 out of 233 patients) (Table 2). Sixteen (6.9 %) and 217 patients (93.1 %) included in Group A and Group B, respectively. Group A patients' age ranged from 53 to 81 years (median 69 years).

Histopathological analysis showed four patients in Stage IIIa (T2N1) and four in Stage IIIb (T2N2, T3N1, T3N2). Colon cancer was diagnosed in three out of 11 patients with emergent segmental colon resection during the index admission. Their stages were Stage IIIa in two patients and Stage IIIb in one patient.

The demographic and clinical features of the patients were similar between the groups except for age. Colon cancer and advanced adenoma were significantly higher in older patients ( $68.1 \pm 8.4$  years and  $57.9 \pm 12.7$  years, respectively) ( $p = 0.001$ ). The patients' grouping based on a cutoff of 50 and 65 years also revealed significant differences ( $p = 0.015$  and  $p = 0.012$ , respectively) (Table 1). There were more patients above 50 and 65 years in group A. Sex, Hinchey classification, and diverticulitis groups were not associated with the development of CSCN ( $p > 0.05$ ).

## Discussion

There was no colon cancer and advanced adenoma in patients below 50 years of age with an ACD attack in the present study. However, the follow-up colonoscopy can be considered in patients older than 50 years due to a 6.9 % rate of CSCN.

In previous studies, an early follow-up endoscopic colon evaluation was recommended after an episode of acute diverticulitis to rule out colorectal malignancy<sup>9,22-25</sup>. After an initial diagnosis of left-sided diverticulitis in all patients, a follow-up colonoscopy was recommended even if the cancer rate was 2.2 % within one year<sup>17</sup>. Several authors concluded that all patients should get a colo-

noscopy to rule out advanced adenoma or adenocarcinoma after an episode of acute diverticulitis<sup>24,25</sup>. Despite these recommendations, evidence-based data was lacking to support the ACD attack as an indication to perform colonoscopy for all patients<sup>4-6,20,26,27</sup>.

The prevalence of colon cancer or advanced adenoma following an attack of ACD was reported to vary from zero to 10.3 %<sup>4,10,17,21,28-32</sup>. The variable results originated from the different inclusion criteria for the patients with acute diverticulitis and definitions used for advanced adenoma and colonic malignancy. In the present study, our detection rates for colon cancer and advanced adenoma were 3.4 % for each, resulting in an overall 6.9 % rate. Besides the similarity of this rate with previous studies, we regard a detection rate of 6.9 % for colon cancer and advanced adenoma as sufficient to recommend a post-ACD colonoscopy.

Several authors tried to specify the most appropriate patient groups for colonoscopy due to low rates of colon cancer during post ACD colonoscopy. Several risk factors were studied, including advanced age, sex, or CT findings. In some studies, age above 50 years was identified as a significant risk factor for clinically significant neoplasia<sup>17-20</sup>. Localization of diverticula in the colon may be essential for such differences<sup>18</sup>. It was also noted the necessity of further research to clarify the requirement of a follow-up colonoscopy for ACD among younger patient populations from the Western countries due to the absence of malignancy in patients below 50 years of age<sup>33</sup>. In agreement with these studies, we did not detect colon cancer and advanced adenoma in patients younger than 50 years. Based on these findings, one could conclude that post-ACD colonoscopy should be performed, aiming to detect possible CSCN, only in patients older than 50 years.

Besides age, other factors, including sex and geographical distribution, may influence these variable outcomes. Male sex is a significant risk factor for colorectal cancer and polyps following ACD attacks<sup>29</sup>. However, there was no significant association between male sex and colon cancer in the present study. There were great differences in clinically significant colonic neoplasia rates between the studies carried out in Western and East-

ern countries<sup>22,34</sup>. Thus, the country of clinical practice could be an essential factor for recommending routine colonoscopy following an episode of ACD.

Complicated diverticulitis is considered a significant risk factor for colon cancer<sup>4,8,10,20-22,29</sup>. Although some authors reported no association between uncomplicated diverticulitis diagnosed as Hinchey 0, 1A, and 1B and colon cancer<sup>29</sup>, we detected one patient with colon cancer staged Hinchey 1b in the present study. It was reported that colorectal cancer risk does not increase after an attack of uncomplicated diverticulitis<sup>8,31</sup>. There were 11 patients with emergent surgical treatment in our study, and colon cancer was detected in three of them. However, contrary to others studies<sup>4,8,20,22,35</sup>, we found no significant association between the modified Hinchey scores and complicated diverticulitis for the development of CSCN. Therefore, the severity of ACD diagnosed using CT may not significantly predict colon cancer risk in all cases.

The cost and potential complications of colonoscopy should be weighed against the potential benefit of detecting an advanced adenoma or colonic malignancy. Several associations have recommended routine colonoscopy after an episode of ACD only in the presence of persistent complaints or alarm symptoms<sup>28,30,35-37</sup>. Many authors avoid performing routine colonoscopy after ACD<sup>4,19,20,27,34-38</sup>. The follow-up colonoscopy is offered as a routine procedure to rule out malignancy based on the previously published guidelines<sup>36</sup>. Therefore, the recommendation of colonoscopy following an episode of ACD remains to be clarified. Current guidelines include controversial recommendations about the necessity of endoscopic follow-up for all ACD patients. The European Society of Coloproctology recommends an endoscopic examination at least six weeks after an acute episode if not performed within the preceding three years<sup>39</sup>. This guideline also mentions that the follow-up colonoscopy in patients with uneventful recovery following a single episode of CT-proven uncomplicated diverticulitis might be regarded as unnecessary. The American Society of Colon and Rectal Surgeons recommends a follow-up colonoscopy after recovering an episode of left-sided complicated diverticulitis<sup>40</sup>. Similar recommendations have been made in the guidelines for acute colonic diverticulitis of the World Society of Emergency Surgery<sup>41</sup>. The current study did not indicate any difference in colon cancer incidence and CSCN between uncomplicated and complicated cases. The age below 50 years might be a critical factor influencing the follow-up colonoscopy decision.

Several authors recommended considering the presence of several suspicious imaging findings for CSCN during CT, including the thickness of the bowel wall exceeding 15 mm and a long clinical course or those with a mass lesion or obstruction on CT scan<sup>4,21</sup>. We regard the presence of these CT findings as indications for evaluating colonic cancer. Still, the inclusion of these patients may cause difficulty assessing the association between ACD and colon cancer, and for that purpose, we excluded such patients.

The retrospective design of the current study is considered a major limitation as the presence of potential alarm symptoms and comorbidities were not able to be evaluated. Also, we lacked patients' follow-up data concerning future ACD attacks or CSCN. Furthermore, excluding a few cases that reduced the number of identified ACD patients by a quarter was another critical limitation. Availability of a relatively small number of patients with colon cancer and CSCN was another non-modifiable factor affecting the reliability of the presented results. We used the modified Hinchey Classification by Wasvary for the severity of acute diverticulitis in the light of previously published papers. This issue may be regarded as a weakness of the study.

In conclusion, routine colonoscopy examination following an episode of ACD in patients younger than 50 years of age may not be necessary to investigate the presence of CSCN. However, the selection of the most appropriate patients for colonoscopic follow-up evaluation after ACD should be clarified by prospective, large-scale studies.

#### Conflict of interest

The authors have no conflicts of interest to declare.

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