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의학석사 학위논문

**Do we need colonoscopy following acute
diverticulitis detected on computed
tomography to exclude colorectal
malignancy?**

전산화 단층 촬영에서 진단된 급성 계실염
환자에서 대장 악성종양을 배제하기 위한
대장내시경의 필요성

2014 년 2 월

서울대학교 대학원

임상의과학과

최 영 훈

A thesis of the Degree of Master of Philosophy

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by
Young Hoon Choi

A thesis submitted to the Department of Clinical Medical
Sciences in partial fulfillment of the requirements for the
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February 2014

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논문 제목: 전산화 단층 촬영에서 진단된 급성 계실염 환자에서 대장내시경의 필요성

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ABSTRACT

Introduction: The aim of this study was to evaluate the yield of colonoscopy for detecting advanced colonic neoplasia in patients treated for diverticulitis detected on computed tomography (CT) and to examine whether subsequent colonoscopy is warranted in patients with diverticulitis on CT.

Methods: The study was composed of patients diagnosed with acute diverticulitis on CT scan from January 2001 to March 2013. Patients who had subsequent colonoscopy within a year from the date of CT were included. For each diverticulitis case, two age- (± 5 years) and sex-matched controls were identified from healthy individuals who had received screening colonoscopy. We evaluated the diagnostic yield of advanced colonic neoplasia in colonoscopy.

Results: One hundred forty-nine patients underwent subsequent colonoscopy within a year from the date of CT. Among the patients, 11 (7.4%) had colon cancer and 7 (4.7%) had advanced adenoma. A case-control study revealed that the odds of detecting an advanced neoplasia among patients with diverticulitis on CT were approximately 8.8 times greater than in the age-, and sex- matched controls [OR, 8.84; 95% CI, 2.90 – 26.96; $P < 0.001$]. On analysis of the diverticulitis group, age (≥ 50 years) is an independent risk factor for detecting advanced colonic neoplasia.

Conclusions: The yield of advanced colonic neoplasia was substantially higher in patients with acute diverticulitis than in asymptomatic, average-risk individuals. Colonoscopy verification is warranted in patients with diverticulitis detected on CT, especially in those aged 50 years or older.

Keywords: diverticulitis, colonoscopy, adenoma, colon cancer

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INTRODUCTION

Over the past few decades, there has been a substantial rise in the prevalence of diverticular disease.(1) Prevalence of diverticular disease rises with age; less than 10% of persons younger than 40 years of age are affected by diverticulosis while over 65% of persons older than age 80 years are affected.(2) Diverticulitis, which results from inflammation of a colonic diverticulum, is the most frequent clinical complication of diverticular disease, affecting 10– 25% of patients with diverticulosis.(3) The prevalence of diverticulitis has increased over the past few decades along with the rise in the prevalence of colonic diverticulosis. Interestingly, the incidence of colon cancer has rapidly increased over the last decades as well. A deficiency of dietary fiber has been suggested as a fundamental factor in the pathogenesis of both diverticulitis and colon cancer.(1) The common etiological factors between both diseases suggest a relatively high incidence of the simultaneous presence of diverticulitis and colon cancer although opposite results have also been published.(2, 4-6)

Computed tomography (CT) is the diagnostic test of choice for diverticulitis patients due to its accurate diagnosis, early identification of complications, and superior definition of bowel wall thickness and extent of extraluminal disease.(7) However, CT features of acute diverticulitis can also be present in colorectal carcinoma. Thus, a malignant lesion of the colon can be diagnosed with a case of diverticulitis.(8) *Bahadursingh* et al reported that 2.6% of patients with acute diverticulitis were subsequently diagnosed with colon cancer.(9) Based on these facts, the American Society of Gastrointestinal Surgery and the American College of Gastroenterology recommend that patients treated for acute diverticulitis undergo colonoscopy to rule out colon cancer.(10-12) However, this recommendation is based on small cohort studies or expert opinions. By contrast, another study suggested that subsequent evaluation of the colon following acute diverticulitis may not be required because the yield of advanced colonic neoplasia was equivalent to or less than that detected on screening asymptomatic, average-risk individuals.(13) In addition, there is concern about the potential risks of colonoscopy, with the most serious complication being perforation at nearly 0.1%.(14) Also, there is a risk of

exacerbation of the disease process, such as turning a sealed perforation into a free one during air insufflation and scope manipulation.(15) Colonoscopy is technically more difficult in diverticular disease due to luminal narrowing, spasm, muscular hypertrophy, and fixation.(16) Therefore, there are controversies regarding the necessity for colonoscopy after management of acute diverticulitis.

The aim of this study was to evaluate the yield of colonoscopy for detecting advanced colonic neoplasia in patients with diverticulitis detected on CT and to examine whether subsequent colonoscopy is warranted in patients with diverticulitis on CT.

METHODS

1. Patient selection

The study protocol was approved by the Institutional Review Board of Seoul National University Hospital and Seoul National University Boramae Medical Center. We reviewed radiology reports containing the word “diverticulitis” on CT at Seoul National University Hospital or Seoul National University Boramae Medical Center from January 2001 to March 2013. We enrolled consecutive patients who underwent CT followed by colonoscopy within a year. The reports were assessed, and patients with acute diverticulitis were identified. Patients with a history of colorectal cancer or colorectal surgery were excluded. Patients who underwent colonoscopy prior one year to diagnosis of diverticulitis were also excluded. The medical record data, including the date of birth, sex, family history of colon cancer, and body mass index (BMI), were obtained. BMI is defined as the individual's body mass (kg) divided by the square of their height (m).

A case-control study was undertaken to determine whether patients who diagnosed diverticulitis on CT was associated with an increased risk of advanced colonic neoplasia. For each diverticulitis case, two age- (± 5 years) and sex- matched controls were identified from healthy individuals who had received screening colonoscopy between January 2001 and March 2013 at Seoul National University Health Care Center. Outcome was estimated by comparing the detection rate for advanced colonic neoplasia between the two groups.

2. Colonoscopy

As mentioned above, we only included the patients who had a colonoscopy within one year from the date of the CT scan. We chose one year to exclude patients who may have developed interval cancers after their diagnosis of diverticulitis. All colonoscopies were performed by board-certified gastroenterologists. All abnormal lesions detected during colonoscopy were biopsied, and if possible, endoscopic mucosal resection was performed. Polyp or mass size was

measured by visual comparison with the open width of the biopsy forceps or was estimated after endoscopic or surgical resection. Positive findings at colonoscopy were defined as advanced colonic neoplasia, such as advanced adenomas, primary colon cancer, or metastasis of primary cancer, including direct invasion. Advanced adenoma was defined as an adenoma ≥ 10 mm size or as an adenoma with a villous component or high-grade dysplasia.

3. Imaging Technique and Analysis

CT scans were performed with a helical multidetector computed tomography (MDCT) system using the standard protocol within the department. Scanning with a slice thickness of 3.8 mm and intravenous (IV) administration of contrast medium was performed for all subjects. Diverticulitis was defined by the presence of colonic diverticula, colonic wall thickening (wall thickness > 3 mm on the short axis of the lumen) and pericolic fat stranding.

4. Statistical analysis

Data analysis was carried out using SPSS 17.0 statistical analysis software (SPSS Inc., Chicago, IL). Patient's demographics and clinical characteristics were expressed as means and as numbers (percentages). Continuous variables were analyzed using Student's t-test and categorical variables were analyzed using the chi-square test. A *P* value of 0.05 was considered statistically significant. Univariate and multivariate logistic regression models were used to estimate the odds of advanced colonic neoplasia.

RESULTS

1. Diverticulitis Patients and CT results

Between January 2001 and March 2013, a total of 1409 CT scans were retrieved from the PACS database (Fig. 1). A total of 443 patients with a CT diagnosis of acute diverticulitis were identified. Of this group, colonoscopy had been performed within a year from the date of CT scan in 149 (33.6 %) patients, and these patients were included in the study. The clinical characteristics of the patients with diverticulitis are summarized in Table 1. The median age was 48.6 ± 16.5 years, and 89 (59.8%) patients were male. There was no significant difference between patients with or without performing colonoscopy.

Figure 1. Patient flow chart summary

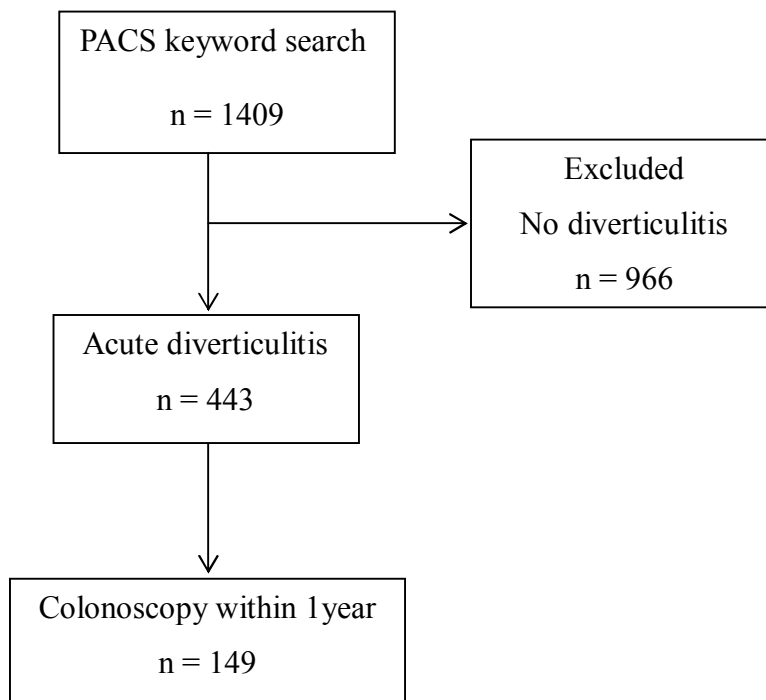


Table 1. Clinical characteristics of diverticulitis patients

	Diverticulitis with colonoscopy (n = 149)	Diverticulitis without colonoscopy (n = 294)	<i>p</i>-value
Age (years), mean±SD	48.6 ± 16.5	46.6 ± 16.6	0.243
Male (%)	59.7	59.9	0.979
Family history of CRC [†] (%)	2.6	3.1	0.806
BMI (kg/m ²), mean±SD	23.3 ± 3.2	22.4 ± 3.2	0.082
Complication [‡] (%)	14.1	8.2	0.051

[†]CRC : colorectal cancer

[‡]Complication : Peritonitis, Obstruction, Perforation, Abscess, Fistula

2. Colonoscopy findings

Colonoscopy findings are listed in Table 2. Overall, 16 patients (10.7 %) with diverticulitis had advanced colonic neoplasia confirmed by colonoscopy and histological evaluation. Among the total number of patients, 11 patients (7.4%) had colon cancer and 7 patients (4.7%) had advanced adenoma. Two patients with colon cancer also had advanced adenoma. Non-advanced adenoma was found in 42 patients (28.2%). There was no significant difference in the prevalence of advanced neoplasia according to the location of diverticulitis. There were no complications associated with colonoscopy.

Table 2. Colonoscopy findings in patients with diverticulitis on CT

Findings	Diverticulitis on Left	Diverticulitis on Right	<i>p</i> -value
	side colon (n=23)	side colon (n=126)	
	Patients No. (%)	Patients No. (%)	
Advanced neoplasia [†]	3 (13.0)	13 (10.3)	0.715
Colon cancer	2 (8.7)	9 (7.1) [‡]	0.679
Advanced adenoma [§]	1 (4.3)	4 (3.2)	0.573
Non advanced adenoma	12 (52.2)	30 (23.8)	0.005
Negative finding	20 (87.0)	112 (88.9)	0.789

[†] Advanced adenoma, primary colon cancer. Metastatic lesion of primary cancer including direct invasion was not detected.

[‡] Two patients also had advanced adenoma.

[§] Advanced adenoma is defined as an adenoma \geq 10mm size or as an adenoma with villous component or high-grade dysplasia. These patients had no malignant lesion.

3. Case-control analysis of risk factors for advanced colonic neoplasia in patients with diverticulitis on CT

We identified 298 age- and sex-matched healthy controls having screening colonoscopy. Diverticulitis patients and control group patients were similar in average age, sex, BMI, and family history of colon cancer. Sixteen patients (10.7%) were diagnosed with advanced colonic neoplasia, including 11 (7.4%) colon cancers in the diverticulitis group. Additionally, four patients (1.3%) were diagnosed with advanced colonic neoplasia, including two with colon cancers (0.7%), in the control group ($P < 0.001$ for advanced colonic neoplasia, $P = 0.001$ for colon cancer) (Table 3).

Table 3. Diagnostic yield of advanced neoplasia in between patients with diverticulitis and healthy controls

	Cases (n=149)	Controls (n=298)	Odds ratio	<i>p</i> -value
	Patients No. (%)	Patients No. (%)	(95% CI)	
Advanced neoplasia [†]	16 (10.7%)	4 (1.3%)	8.84 (2.90 – 26.96)	< 0.001
Advanced adenoma [‡]	5 (3.4%)	2 (0.7%)	5.14 (0.99 - 26.81)	0.052
Colon cancer	11 (7.4%) [§]	2 (0.7%) [¶]	11.80 (2.58 – 53.95)	0.001

[†] Advanced adenoma or primary colon cancer. Metastatic lesion of primary cancer including direct invasion was not detected.

[‡] Advanced adenoma is defined as an adenoma ≥ 10 mm size or as an adenoma with villous component or high-grade dysplasia. These patients had no malignant lesion.

[§] Two patients also had advanced adenoma.

[¶] One patient also had advanced adenoma.

4. Risk factors for advanced colonic neoplasia in patients with diverticulitis on CT

We performed an analysis according to the presence of complications related to diverticulitis. However, there was no significant difference between the diverticulitis and control groups (Table 4). We also performed an analysis according to age. As shown in Table 5, advanced lesions were found in patients 50 years of age or older. There was a significant difference in the prevalence of advanced lesions, including colon cancer, between those aged 50 years or older and those younger than age 50. We next performed a multivariate logistic analysis, which identified age (≥ 50 years) as an independent risk factor for advanced lesions among patients with diverticulitis on CT (Table 6).

Table 4. Diagnostic yield of advanced neoplasia in patients with complicated diverticulitis vs. uncomplicated diverticulitis

	Complicated diverticulitis (n = 21) Patients No. (%)	Uncomplicated diverticulitis (n = 128) Patients No. (%)	p-value
Advanced neoplasia [†]	4 (19.0)	12 (9.4)	0.245
Colon cancer	3 (14.3)	8 (6.3) [‡]	0.188
Advanced adenoma [§]	1 (4.8)	4 (3.1)	0.537

[†] Advanced adenoma, primary colon cancer. Metastatic lesion of primary cancer including direct invasion was not detected.

[‡] Two patients also had advanced adenoma.

[§] Advanced adenoma is defined as an adenoma ≥ 10 mm size or as an adenoma with villous component or high-grade dysplasia. These patients had no malignant lesion.

Table 5. Diagnostic yield of advanced neoplasia according to the patient's age

	Age more than 50 (n=71)	Age under 50 (n=78)	<i>p</i> -value
	Patients No. (%)	Patients No. (%)	
Advanced neoplasia [†]	14 (19.7)	2 (2.6)	0.001
Colon cancer	11 (15.5) [‡]	0 (0.0)	< 0.001
Advanced adenoma [§]	3 (4.2)	2 (2.6)	0.669

[†] Advanced adenoma, primary colon cancer. Metastatic lesion of primary cancer including direct invasion was not detected.

[‡] Two patients also had advanced adenoma.

[§] Advanced adenoma is defined as an adenoma \geq 10mm size or as an adenoma with villous component or high-grade dysplasia. These patients had no malignant lesion.

Table 6. Univariate and multivariate analysis for advanced colonic neoplasia in patients with diverticulitis detected on CT

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	<i>p</i> -value	OR (95% CI)	<i>p</i> -value
Age (≥ 50)	9.33 (2.04-42.71)	0.004	9.13 (1.97-42.27)	0.005
Male	1.14 (0.39-3.32)	0.811	1.08 (0.35-3.34)	0.901
Complication [†]	2.28 (0.66-7.87)	0.194	1.96 (0.52-7.40)	0.323
LNE [‡]	0.81 (0.17-3.83)	0.787	0.97 (0.19-4.99)	0.968
Hematochezia	1.41 (0.16-12.53)	0.757	0.88 (0.09-8.59)	0.912

[†]Complication : Peritonitis, Obstruction, Perforation, Abscess, Fistula

[‡]LNE : Lymph node enlargement of mesenteric or retroperitoneal lymph node

DISCUSSION

Our study, which included multicenter patients who had undergone CT and subsequent colonoscopy, investigated the need for colonoscopic verification in patients with diverticulitis detected by CT. Sixteen patients with diverticulitis on CT had advanced colonic neoplasia including 11 colorectal cancers. This result suggests that a substantial proportion of patients with diverticulitis on CT had advanced colonic neoplasia including malignancy.

A recent review regarding the management of patients with diverticulitis detected on CT indicates that colonoscopy is recommended.(11) However, direct evidence for the need of colonoscopy is lacking. In addition, previous studies have produced controversial results.(17, 18) Furthermore, colonoscopy-related complications, such as perforation, can lead to morbidity and mortality. Therefore, we performed a study to determine whether colonoscopy verification is required in patients with diverticulitis detected on CT. The yields of advanced colonic neoplasia in the diverticulitis group and control group were 10.7% and 1.3%, respectively. We confirmed 16 advanced colonic neoplasms, including 11 primary colon cancers and performed colonoscopy without significant complication. The odds of detecting an advanced neoplasia among patients with diverticulitis on CT were approximately 8.8 times greater than in the age-, and sex- matched controls. Therefore, we think that our data provide valuable information regarding the prevalence and risk of advanced colonic neoplasia in patients with diverticulitis detected on CT.

Several studies have reported results regarding colonoscopy after diverticulitis.(13, 19, 20) The yields for advanced lesions were varied. One study reported that the prevalence of colonic neoplasia and colon cancer were 5.4% and 0.3%, respectively, among 292 patients with acute uncomplicated diverticulitis.(13) In another study of, 423 patients who were conservatively treated for diverticulitis, the yield of colon cancer was 1.9%.(19) A third study, involving 1088 patients with left-sided diverticulitis, determined the yield of colon cancer to be 2.1%.(20) Therefore, our data showed a higher prevalence of colonic neoplasia compared to previous studies. We think there are several reasons for this. First, we selected patients who had

colonoscopy for the diagnosis of colorectal neoplasia in patients with diverticulitis. In one of the previous studies, only 319 of 1088 patients underwent colonoscopy, and the presence of cancer in other patients was confirmed by cancer registry.(20) Other studies(13, 19) included a number of patients who had barium enema or sigmoidoscopy. Second, we carefully excluded patients who underwent colonoscopy prior one year from index date of diverticulitis. Finally, we included patients with complicated diverticulitis because a previous study showed a significant correlation of complicated diverticulitis with colon cancer.(21) A recent study reported that the prevalence of clinically significant neoplasia on colonoscopy after management of acute diverticulitis is 9.2%, which is consistent with our result.(22) Therefore, we believe that our data provide a more precise prevalence of advanced colonic neoplasia in patients with diverticulitis on CT.

A recent study showed that patients with complicated diverticulitis had a significantly higher incidence of advanced colonic neoplasia in comparison with patients who presented with uncomplicated diverticulitis.(22) However, in our study, there was no significant difference between patients with complicated diverticulitis and patients with uncomplicated diverticulitis. One possible reason for this is that we had a smaller proportion (14.1%) of patients with complicated diverticulitis than in the previous study (29.7%).(22) In addition, the previous study included only complicated diverticulitis cases with abscess because patients with complicated diverticulitis with fistula underwent surgery, which could have resulted in selection bias.(22) In the present study, age 50 years or older showed a significantly increased prevalence of advanced neoplasia as compared to those under age 50. This remained significant when adjusting for important variables. Several guidelines recommend screening for colorectal cancer using various modalities beginning at age 50 years.(23-25) Based on our results, patients with diverticulitis, especially those age 50 years or older, need colonoscopy verification to exclude underlying advanced colonic neoplasia.

We think that our study has several strengths compared to previous studies. This was the first multi-center cohort analysis of colonoscopy following diverticulitis detected on CT. Through the design of the study, we were able to deliberately minimize the bias arising from a single

center study design. We included patients who underwent colonoscopy within a year after index date of CT, thereby precise measurement of the prevalence of colonic neoplasia was possible. Third, we provided evidences of the need for colonoscopy in patients with diverticulitis on CT through a case-control study and multiple logistic regression analysis. Finally, to our knowledge, this is the first study of its kind performed in East Asian patients, suggesting that the yield of advanced neoplasia in patients with diverticulitis detected on CT is similar to Western populations.

Our study has several limitations. First, it is limited by its retrospective design. Second, not all patients undergoing CT had subsequent colonoscopy, which may have affected our assessment of the precise prevalence of colonic neoplasia. Our study might have enrolled an unusually higher proportion of patients with advanced neoplasia because of selection bias. However, we believe that our data minimized bias because all patients enrolled in this study underwent colonoscopy, providing a precise yield of advanced lesions, and the characteristics of patients who did not have colonoscopy were not significantly different. Nevertheless, our data should be interpreted with caution because of the retrospective study design. A prospective cohort study that includes a large number of patients is needed to determine whether diverticulitis on CT warrants endoscopic verification.

In conclusion, the yield of advanced colonic neoplasia in this cohort was substantially higher than that detected on screening asymptomatic average-risk individuals. Colonoscopy verification is warranted in patients with diverticulitis detected on CT, especially those whose age is 50 years or older.

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국문 초록

서론: 대장 계실염의 치료 후 기저 악성질환을 배제하기 위해 대장내시경을 시행하고 있지만 이를 뒷받침할만한 근거는 부족한 실정이다. 이에 대장 계실염 치료 후 시행한 대장내시경을 통해 진단되는 악성질환의 비율에 대해 알아보고, 전산화 단층 촬영에서 진단된 대장 계실염 환자에서 대장내시경의 필요성에 대해 알아보고자 하였다.

방법: 2001 년 1 월부터 2013 년 3 월 사이에 전산화 단층 촬영에서 계실염으로 진단된 환자 중 전산화 단층 촬영 1 년 이내에 대장내시경을 시행한 환자들을 대상으로 하였다. 각각의 계실염 환자에 대해 건강검진으로 대장내시경을 시행받은 사람 중 두 명씩을 짝지어 대조군으로 설정하였고, 대장내시경을 통한 진행성 대장 신생물의 진단율에 대해 평가하였다.

결과: 전산화 단층 촬영에서 진단된 계실염 환자 중 1 년 이내에 대장내시경을 시행한 환자 수는 149 명이었다. 이 중 11 명 (7.4%)의 환자가 대장암, 7 명 (4.7%)의 환자가 진행성 선종으로 진단되었다. 환자 대조군 분석에서 진행성 대장 신생물의 진단에 대한 대응비는 계실염 환자군에서 대조군에 비해 약 8.8 배 [대응비, 8.84; 95% 신뢰구간, 2.90 - 26.96; $P < 0.001$] 높았다. 계실염 환자군 분석에서는 50 세 이상의 나이가 진행성 대장 신생물을 발견하는데 독립적인 위험인자로 밝혀졌다.

결론: 급성 계실염 환자군에서 진단된 진행성 대장 신생물의 비율은 무증상의 평균적인 대장암의 위험도를 가진 대조군에 비해 유의하게 높았다. 이에 전산화 단층 촬영에서 진단된 계실염 환자, 특히 50 세 이상의 환자에서 대장내시경을 통한 평가가 필요하다고 생각된다.

주요어 : 계실염, 대장내시경, 선종, 대장암

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