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World J Gastroenterol 2007 March 21; 13(11): 1646-1651
World Journal of Gastroenterology ISSN 1007-9327

GASTRIC CANCER

Role of computed tomographic colonoscopy of postoperative surveillance in patient with gastric cancer

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Received: 2007-01-18 Accepted: 2007-03-16

Abstract

AIM: To examine the diagnostic yield of colorectal neoplasia at computed tomographic colonoscopy (CTC) as well as the feasibility of contrast enhanced CTC in patients with gastric cancer.

METHODS: To examine the incidence of colon polyp we selected postoperative 188 gastric cancer patients, which we refer to as the 'colon polyp survey group'. To examine the feasibility of CTC for early detection of colon cancer or advanced colon adenoma, we selected 47 gastric cancer patients (M:F 29:18, mean age 53.8 years), which we call the 'CT colonoscopy group'. All the 47 patients underwent successive CTC and colonoscopy on the same day.

RESULTS: Totally 109 colon polyps were observed from 59 out of 188 gastric cancer patients, the incidence rate of colon polyps in gastric cancer patients being 31.4%. The sensitivity of CTC in detecting individuals with at least 1 lesion of any size was 57.1%, the specificity was 72.7%, the positive predictive value was 47.1%, and the negative predictive value was 71.9%. When the cutoff size was decreased to 6 mm, the sensitivity and specificity were 80.0% and 92.9%, respectively, with positive and negative predictive values of 57.1% and 97.5%, respectively. Only one patient was classified as false negative by virtual colonoscopy.

CONCLUSION: The diagnostic yield of colorectal polyp was 31.4% in patients with gastric cancer, and contrast enhanced CTC is an acceptable tool for the detection of synchronous colorectal advanced adenoma and postoperative surveillance of gastric cancer patients.

Key words: Stomach cancer; Colon cancer; Computed tomographic colonoscopy

Jun DW, Lee OY, Lim HC, Kwon SJ, Lee HL, Yoon BC, Choi HS, Hahm JS, Lee MH, Lee DH. Role of computed tomographic colonoscopy of postoperative surveillance in patient with gastric cancer. *World J Gastroenterol* 2007; 13(11): 1646-1651

http://www.wjgnet.com/1007-9327/13/1646.asp

INTRODUCTION

Gastric cancer is the most common form of cancer in Korea. Majority cancer patients are of old age, especially the mean age of stomach cancer patients is 54 in Korea[1]. As the survival rate has increased remarkably owing to an early detection of gastric cancer and improvement in treatment results, its relation with colon cancer and second primary cancer in patients with gastric cancer has become the subject of much interest. Stomach and colon cancers share the genetic abnormalities such as p53[2], APC[3], DCC[4], and K-ras[5] and genetic instability including microstellite instability[6]. According to previous studies, 3.4%-4.2% of patients with gastric cancer had synchronous or metachronous cancer, the type of which is predominantly colorectal[7,8]. Yoo *et al*[9]. suggested the necessity of colonoscopy before or after gastric cancer surgery as the prevalence of colon cancer is significantly high after correction of age and sex of patients with gastric cancer in recent multi-center study results. Therefore, colonoscopy is expected to play an important role in identifying synchronous colon cancer or advanced adenoma in patients with gastric cancer before or after surgery. Of course, colonoscopy is the golden standard method for an early identification of colorectal cancer. Colonoscopy is, however, very difficult to perform especially after gastric cancer surgery, because most patients are very old and generally have low body mass index due to the surgery and their past history of abdominal surgery affects the completion rate in colonoscopy[10]. After the cancer surgery, almost all

cancer patients participated in the follow up gastroscopy and radiologic imaging study, including the computed tomography according to the follow up schedule. Lately, studies on feasibility of computed tomographic colonoscopy (CTC) by colon cancer screening have been reported[11,12]. This led us to think the contrast enhanced CTC after gastric cancer surgery may be helpful to evaluate postoperative metastasis as well as to find metachronous tumor or advanced colon adenoma.

This study aims at examining the diagnostic yield of colorectal neoplasia at CTC as well as the feasibility of contrast enhanced CTC in patients with gastric cancer.

MATERIALS AND METHODS

Subjects

We retrospectively analyzed their colonoscopy findings from June 2003 to December 2006 to estimate the diagnostic yield of colorectal neoplasia in gastric cancer patients. A total of 188 patients out of 871 who had gastric cancer surgery that underwent colonoscopy within 1 year after surgery were selected for our study. This group of the patients is called the 'colon polyp survey group'.

Routine follow up abdominal computed tomography was done at 6 mo after surgery. At that time, contrasted enhanced CTC and conventional colonoscopy were taken on the same day to investigate the feasibility of contrasted enhanced CTC in post gastrectomy patients from January to December 2006. This group of the patients is called the 'CT colonoscopy group'. 55 patients in the 'CT colonoscopy group' took 4 liters of colonic washing fluid in the evening before the CTC and had CTC between 9:00 and 10:00 the next day. Conventional colonoscopy was performed between 14:00 and 15:00. At the time of their entry into the programs they were given written consent forms with information. All the eligible 55 patients completed detailed questionnaires which encompass demographics, gastrointestinal symptoms, past medical history, and degree of pain or discomfort.

Virtual colonoscopy

All the patients had contrasted enhanced CTC prior to same-day colonoscopy. Patients were placed in decubitus position either for enema tip insertion or for slow manual insufflation of approximately 2 L of air (until the patient verbally indicated air administration had reached maximal tolerance). Both supine and prone data acquisitions were obtained. A sixteen slice multi-detector row CT (Somatom sensation 16, Siemens, Forchheim, Germany) was used. The CT technique involved the use of 0.75 mm collimation, a table speed of 15 mm/s a reconstruction interval of 0.5 mm, and scanner settings of 100 mA and 120 kVp. Image processing and interpretation were performed with the use of a commercially available CT colonographic system (Rapidia, LG Infinity). This software program extracts the images of the air-filled colon, generates an automated centerline for luminal navigation, and electronically removes from images the opacified residual fluid in a routine postprocessing step.

Conventional colonoscopy

Colonoscopy was performed in the standard fashion to examine the entire colorectum by one experienced colonoscopist who was initially unware of the results of the virtual colonoscopy. After the colonoscopist completed the evaluation of a given segment of the colon, a study coordinator revealed the results of the virtual colonoscopy for the previously examined segment. If a polyp measuring 5 mm or more in diameter was seen on virtual colonoscopy but not on the initial optical colonoscopy, the colonoscopist closely reexamined that segment and was allowed to review the images obtained on virtual colonoscopy for guidance. Polyp size was estimated using an open biopsy forceps.

Questionnaire

They were first asked whether they experienced any pain or discomfort during the procedure and which procedure they prefer. Those who reported pain or discomfort were asked to rate their pain on a 100 mm VAS (visual analogue scale). The VAS was labeled "no pain/discomfort" on the left end and "pain/discomfort as bad as it could be" on the right end.

Statistical analysis

All statistical analyses were performed using the SPSS 11.0 statistical package.

Categorical data were analyzed using the chi-square test (Fisher's exact test). Continuous data were analyzed using the Student's t-test and one-way ANOVA (Scheffe's test). To minimize type I error, $P < 0.05$ was considered statistically significant.

RESULTS

Patient characteristics

Of 188 patients who belonged to the 'colon polyp survey group' 117 were males (62.2%) and 71 females (37.8%). The mean age of the patients was 60.1 yr, and 82 patients (43.6%) were in Stage Ia and majority of the patients (125 patients, 66.4%) were tubular adenocarcinoma according to histological findings.

Of 55 belonged to the CT colonoscopy group, 47 underwent complete examinations. Seven patients were excluded because of incomplete colonoscopy for severe adhesion and redundancy (for the rate of completion of 87.3%). Only one patient was excluded because of failure of the CT colonographic system. Among the 47 selected patients, which consisted of 29 males (61.7%) and 18 females (38.3%) with the mean age of 53.8 (range: 29-80) years, 27 had early gastric cancer, and 20 had advanced gastric cancer, while 34 underwent the subtotal gastrectomy, and 13 the total gastrectomy. The mean follow up period was 23.2 (range 6-96) mo (Table 1).

Colon polyp in gastric cancer patients

A total of 109 colon polyps were observed from 59 out of the 188 gastric cancer patients, the incidence rate of colon polyps in gastric cancer patients being 31.4%. 11 (5.9%) out of the 59 patients had more than 3 multiple polyps.

Table 1 Baseline characteristics of the subjects

Characteristics	Colon polyp survey group *n* = 188 (%)	CT colonoscopy group *n* = 47 (%)
Male	117 (62.2)	29 (61.7)
Female	71 (37.8)	18 (38.3)
Age (yr)		
Mean	60.1	53.8
Range	38-80	29-80
TMN Stage		
Ⅰa	82 (43.6)	23 (48.9)
Ⅰb	41 (21.8)	9 (19.1)
Ⅱ	29 (15.4)	5 (10.6)
Ⅲa	16 (8.5)	5 (10.6)
Ⅲb	11 (5.9)	4 (8.5)
Ⅳ	9 (4.8)	1 (2.1)
Operation		
Mucosectomy	1 (0.5)	0 (0.0)
Subtotal gastrectomy	152 (80.9)	34 (72.3)
Total gastrectomy	35 (18.6)	13 (27.7)
Interval from operation		
Mean (mo)	40.8	23.2

Table 2 Colon polyp number and prevalence in colon polyp survey group and CT colonoscopy group

Characteristics	Colon polyp survey group *n* = 188 (%)	CT colonoscopy group *n* = 47 (%)
Number of total colon polyps	109	20
1	35	10
2	13	5
3	5	0
4	2	0
5	3	0
> 5	1	0
Prevalence of colon polyp	59 (31.4%)	15/47 (31.9%)
Success rate of cecal intubation	91.50%	83.70%

Table 3 Characteristics of colorectal lesions confirmed by colonoscopy in CT colonoscopy group

	Total (*n* = 20)	Adenoma	Hyperplasia
Size			
1-5 mm	15	11	4
6-9 mm	2	1	1
⩾ 10 mm	3	3	0
Location			
Rectum	6 (30%)	5	1
Sigmoid colon	7 (35%)	6	1
Descending colon	1 (5%)	1	0
Transverse colon and splenic flexure	3 (15%)	3	0
Ascending colon and hepatic flexure	2 (10%)	0	2
Cecum	1 (5%)	0	1

A total of 20 polyps were observed from 15 patients out of 47 (31.9%) belonging to the 'CT colonoscopy group'. But in the CTC findings, a total of 25 polyps were seen in 14 patients. 15 polyps were diminutive, less than 5 mm, 2 were 6-9 mm, and 3 were greater than 10 mm found from patients with advanced adenoma (Table 2). Colon polyps had histological findings as follows; adenoma, 15 (75%); and hyperplastic 5 (25%). Distribution of lesions was as follows; rectum, 6 (30%), sigmoid, 7 (35%); descending, 1 (5%), transverse, 3 (15%), ascending, 2 (10%); and cecum 1 (5%). Lesions larger than 10 mm in diameter were seen at the rectum, descending, and transverse colon and all the lesions were confirmed as an adenomatous polyp in histology (Table 3).

Patient Detection in CTC

The sensitivity of virtual colonoscopy in detecting individuals with at least 1 lesion of any size was 57.1%, the specificity was 72.7%, the positive predictive value was 47.1%, and the negative predictive value was 71.9% (Table 4). When the cutoff size was decreased to 6 mm, the sensitivity and specificity were 80.0% and 92.9%, respectively, with positive and negative predictive value of 57.1% and 97.5%, respectively. Only one patient was classified as false negative by virtual colonoscopy.

Individual detection in CTC

Virtual colonoscopy correctly identified 12 lesions of the 25 lesions seen on conventional colonoscopy for an overall sensitivity of 60.0%. The sensitivity of virtual colonoscopy in detecting lesions varied depending on the size of the lesion; 100% for lesions larger than 10 mm, 80% for lesions between 6 and 9 mm, and 46.2% for lesions smaller than 6 mm (Table 5). Virtual colonoscopy failed to detect 8 lesions that were classified as false negative. The majority of missed lesions were smaller than 5 mm in size. Only one lesion measuring larger than 5 mm in diameter was classified as a false negative lesion. All 13 lesions were classified as false positive lesions. The majority of false positive lesions were smaller than 5 mm in size and most of them were confused with air bubbles (Table 5).

Questionnaire for abdominal discomfort

A total of 40 of the 47 patients returned their post-study questionnaires (85.1 percent) during procedure. Overall, more patients recalled greater discomfort associated with virtual colonoscopy (16 patients, 40.0%) than with optical colonoscopy (13 patients, 32.5%); 7 patients (17.5%) were undecided as both studies were equivalent to them with regard to discomfort; 4 patients (10.0%) couldn't remember it because of retrograde of amnesia. However, the mean VAS score of reported pain or discomfort was 39.2 ± 28.6 for conventional colonoscopy group, and 44.8 ± 24.1 for virtual colonoscopy group. There was no significant difference between two groups (Figure 1). The same number of patients, 16 (40.0% each), indicated their preference for virtual colonoscopy and for conventional colonoscopy for future screening. 8 patients (20.0%) had no preference or were undecided (Figure 2).

DISCUSSION

As the survival rate has recently increased owing to an early identification of gastric cancer and improvement in treatment results, the second primary cancer in patients with gastric cancer has received much attention. The

Table 4 Ability of virtual colonosocpy to identify patients with colorectal polyps or masses according to lesion in CT colonoscopy group

	TP (*n*)	TN (*n*)	FP (*n*)	FN (*n*)	Sensitivity	Specificity	PPV	NPV
⩾ 1 mm	8	24	9	6	57.10%	72.70%	47.10%	80.00%
⩾ 6 mm	4	39	3	1	80.00%	92.90%	57.10%	97.50%

TP: true positive, TN: true negative, FP: false negative, FN: false negative, PPV: positive predictive value, NPV: negative predictive value.

Table 5 Results of virtual colonoscopy comparing with colonoscopy according to polyp size in CT colonoscopy group

Size	No. of polyp	True positive	False negative	Sensitivity (%)
⩾ 10 mm	2	2	0	100
6-9 mm	5	4	1	80
1-5 mm	18	6	7	46.2
All	25	12	8	60

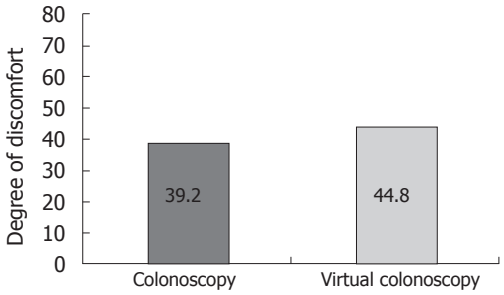

Figure 1 Degree of abdominal discomfort during conventional colonoscopy and virtual colonoscopy.

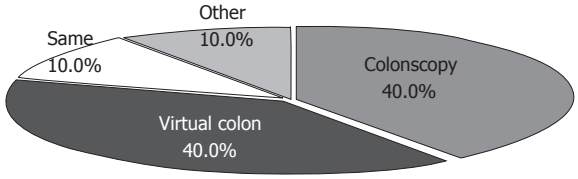

Figure 2 Overall preference between conventional colonoscopy and virtual colonoscopy.

second primary cancer influences the prognosis of gastric cancer patients. The detection of synchronous or metachronous cancer gives us the opportunity to treat both the gastric and second primary cancers simultaneously and thus to beneficially influence the prognosis and quality of life. Therefore, both preoperative and postoperative screenings for second primary cancers should be performed. According to the previous few reports, the incidence that patients with gastric cancer have second primary cancer is substantially high[13]. Ikeda *et al*[14]. analyzed 2250 patients and reported 95 (4.2%) had synchronous or metachronous second primary cancer with colorectal cancer most prevalently occurring (32.5%) . In Korea, Lee *et al*[7]. analyzed retrospectively 3291 gastric patients and reported 3.4% had synchronous cancer again with colorectal cancer most prevalently occurring (37.2%). It may be difficult, however, to explain directly the risk of colon cancer or incidence of colon polyp in gastric cancer patients, as most of studies were retrospective and majority of the patients did not have colonoscopy. In the recently performed prospective multi-center trial study[9], 723 gastric cancer patients had colonoscopy and the incidence rate of colon cancer was 2.42%, meaning it is 2.5 times that of healthy people (0.97%). Especially in case of patients in their fifties or less, 3.52% of gastric cancer patients had also colon cancer, as many as 11 times the rate of the healthy control group (0.33%). In our study, colon cancer was not seen, but colon polyps were observed from 172 patients (31.4%). There are very few data on the prevalence of polyp in healthy adults in Korea, but the number was higher than 21.3% which was the prevalence of polyp in healthy adults with no symptoms who were in the same hospital at a similar time[15], and higher than 23.9% which was reported by Park *et al*[16] who performed the study with 17 468 patients in the tertiary hospital. In the study of Park *et al*[16]. the mean age of the patients was 52.3 years, but most of patients (12 941 patients, 73.8%) were transferred to the tertiary hospital with warning symptoms such as bowel habit change, stool caliber change, anemia, weight loss, etc. In spite of lots of limitations in this study design, the incidence of colon polyp in patients with gastric cancer shows higher rate than previous studies.

Until now the golden standard method for early detection of colon cancer has been colonoscopy. However, colonoscopy has substantial drawbacks as a screening test, such as the need to insert an intravenous catheter for the administration of sedatives, a recovery time of 30 to 60 min, and the requirement for a driver to accompany the patient home. The total time for admission, the performance of the procedure, and subsequent monitering is approximately two hours. Moreover, CTC is a very useful method to determine postoperative recurrence and identify metachronous cancer, especially colon advanced adenoma, considering that most patients are old and generally have low body mass index due to surgery and almost all of them are expected to take the abdomen CT for regular follow up. In our study, the performance of virtual colonoscopy in identifying patients with colorectal lesions correlated positively with the cutoff size used. Virtual colonoscopy had a high sensitivity (80.0%) and specificity (92.9%) in detecting individuals with lesions of size 6 mm or greater. Our results compare with published studies reporting sensitivities of 43%-94% and specificities of 92% in identifying patients with lesions 6-9 mm polyp[17-21]. Our most impressive finding was the very high negative predictive values for all size cutoffs over 6 mm. The strong negative predictive value of virtual colonoscopy

Table 6 Frequency of age, stage, and histology type according to colon polyp.

	Polyp		*P*
	Yes *n* (%)	No *n* (%)	
Age			
< 39	0 (0.0)	1 (100.0)	0.006
40-49	3 (14.3)	18 (85.7)	
50–59	17 (25.8)	49 (74.2)	
60–69	26 (36.6)	45 (63.4)	
> 70	13 (44.8)	16 (55.2)	
Histology			
Papillary	1 (50.0)	1 (50.0)	0.073
Tubular; Well differentiation	4 (25.0)	12 (75.0)	
Moderate differentiation	26 (42.6)	35 (57.4)	
Poorly differentiation	14 (29.2)	34 (70.8)	
Signet ring	10 (19.2)	42 (80.8)	
Mucinous	1 (16.7)	5 (83.3)	
Mixed	1 (50.0)	1(50.0)	
Miscellaneous	0 (0.0)	1 (100.0)	
Stage			
Ⅰ	35 (28.5)	88 (71.5)	0.546
Ⅱ	18 (62.1)	11 (37.9)	
Ⅲ	15 (55.6)	12 (44.4)	
Ⅳ	8 (88.9)	1 (11.1)	

$P < 0.05$ chi-square test.

may preclude the need for more invasive conventional colonoscopy in the vast majority of individuals undergoing colorectal cancer screening. In our study population, the prevalence of lesions of any size was 29.8%, lesions greater than 6 mm was 8.5%, and lesions 1 cm or greater was 4.3%. As seen in other studies, our results showed that virtual colonoscopy fared poorly in detecting individual lesions and patients with lesions 5 mm or less. However, the prevalence of malignancy in diminutive polyps is extremely small, approximating 0.25%[22-24].

Previous study showed virtual colonoscopy more acceptable in terms of overall convenience[11]. But our result showed degree of discomfort between two groups was not statistically different (39.2 *vs* 44.8) and the overall preference between conventional colonoscopy and CTC was the same. Of course there are some methodological problems. At first, it is difficult to direct compare the degree of associating abdominal symptoms because two procedures were done successively. And in our study air insufflation was performed to the maximal level tolerated by the patient during the CT colonoscopy.

We also investigated the factors affecting incidence of colon adenoma. It increased more and more with advance in age (Table 6). However, there was no significant difference of adenoma prevalence according to pathology type (tubular adenoma, signet ring cell and papillary cell type.) and TMN stage. Our results show the tendency that prevalence of colorectal polyp increased in patients with gastric cancer, and CTC is an acceptable tool for the detection of synchronous or metachronous colorectal advanced adenoma in gastric cancer patients.

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