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OBSERVATIONAL STUDY

Laterally spreading tumors: Limitations of computed tomography colonography

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Abstract

AIM: To prospectively investigate the detection rate of laterally spreading tumors (LSTs) of the colorectum by computed tomography (CT) colonography (CTC).

METHODS: Patients with LSTs measuring ⩾ 20 mm detected during colonoscopy were prospectively enrolled in the study. All patients underwent colonoscopy and subsequent CTC on the same day. CTC was performed using multi-detector CT without contrast in the prone and supine positions. Two radiologists blinded to the existence of LSTs read the virtual endoscopic images as well as 2-D images. LSTs were classified into granular and non-granular types based on colonoscopic appearance.

RESULTS: Forty-seven pathologically proven LSTs were evaluated prospectively. Histology included adenomas in 19, mucosal cancers in 19 and T1 cancers in 9. The mean diameter of the LSTs was 35.1 mm. Twenty-eight (60%) LSTs were correctly identified by CTC, and the configuration was similar to the colonoscopic appearance in most cases. Detection rate for the granular type was significantly higher than that for the non-granular type (71% *vs* 31%, $P = 0.013$). Detection rate of adenomas was significantly lower than mucosal cancers (32% *vs* 79%, $P = 0.008$) and T1 cancers (32% *vs* 78%, $P = 0.042$).

CONCLUSION: The detection rate of LSTs by CTC, particularly the non-granular type was not acceptable. Practitioners should be aware of the relatively low detection rate when using CTC.

Key words: Computed tomography colonography; Laterally spreading tumor; Colon neoplasm; Advanced lesion; Flat adenoma; Detection rate

Core tip: Laterally spreading tumors (LSTs) are a major target for colon screening. Nevertheless, it is still unknown what percentage of LSTs can be identified with computed tomography (CT) colonography (CTC). It has been reported that CTC may miss flat neoplastic lesions regardless of their size. It is a fascinating clinical question whether non-granular type LSTs, which have a very flat appearance on optical colonoscopy, can be identified with CTC. This study demonstrated that the detection rate of LSTs by CTC, particularly the non-granular type was not acceptable. Practitioners should be aware of the relatively low detection rate when using CTC.

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INTRODUCTION

Laterally spreading tumors (LSTs) in the large intestine are defined as an epithelial neoplasm measuring 1cm or greater with a low vertical axis that extends laterally along the luminal wall[1-4]. Histologically, more than 30% of LSTs contain high-grade dysplasia or invasive cancer[1,3]. Therefore, LSTs represent advanced lesions[5], and constitute a major target for colon screening. LSTs are divided into two subtypes based on their endoscopic morphology[1,2]. The LST polypoid type is referred to as the LST granular type (LST-G), whereas the LST non-polypoid type is referred to as the LST non-granular type (LST-NG). LST-NG have a biologically aggressive nature with a submucosal invasion rate higher than that of LST-G[1,3,4].

CT colonography (CTC) is an alternative to optical colonoscopy in a colon screening program[6]. Polyps measuring 1 cm or greater are identifiable by CTC with a greater than 90% detection rate[7,8]. However, it has been reported that flat adenomas can be easily missed with CTC[9]. Since the majority of LSTs show a flat appearance regardless of their diameter, it is still unknown what percentage of LSTs can be identified with CTC, thus being a key question to be addressed in a clinical trial. The aim of this study is to prospectively investigate the detection rate of LSTs by CTC.

MATERIALS AND METHODS

Patients and lesions

Prior to commencement, the study was approved by the Institutional Review Board, and was registered at UMIN Clinical Trial Registry (ID: UMIN000002755). In April 2008 and February 2010, patients with LSTs measuring approximately 2 cm or greater on colonoscopy at Jichi Medical University Hospital were prospectively enrolled. The definition of LSTs is according to previous reports[1-4]. The morphology of LSTs was classified into LST-G and LST-NG based upon colonoscopic appearance. Written informed consent was obtained after colonoscopy if the lesion was suspicious for a LST measuring 2 cm or greater based on colonoscopic findings. Since accurate measurement of the diameter could not be made during colonoscopy, the final study group includes patients with lesions smaller than 2 cm as shown on the resected specimen. Lesions mimicking LSTs based on colonoscopic findings but invading to the muscularis propria or beyond were excluded from analysis.

CTC procedure

Patients underwent bowel preparation with 2 litters of polyethylene glycol lavage solution (Niflec®, Ajinomoto Pharma, Tokyo, Japan) or 1.8 L of magnesium citrate solution (Magcorol P®, Horii Pharma, Tokyo, Japan). Prior to CTC, patients underwent conventional colonoscopy after administration of 10 mg of scopolamine butyl bromide or glucagon, but without sedation. Instead of electric cleansing with fecal tagging, the mucosal surface was cleansed by washing, particularly in the area where the lesions were located, and the luminal liquid aspirated as much as possible during colonoscopy. Biopsy specimens were not taken from the lesions. CTC was performed by 40-row or 64-row multi-detector CT immediately after colonoscopy. All patients were placed in the left lateral decubitus position, and an enema tube inserted into the anus. Room air was gently insufflated into the colon until the patient had abdominal distension. A standard scout image was obtained to assess colonic distension. The patient did not receive any contrast medium. CTC scans were obtained by MDCT (Sensation 40 or Definition; SIEMENS, Forchheim, Germany) with the patient in the prone and supine positions. The CT technique involved the use of 40 mm or 64 mm × 0.6 mm collimation, a slice width of 1.25 mm, a reconstruction interval of 1.0 mm, pitch of 0.9 and scanner settings of 120 kVp and 200 mAs.

Image analysis

Prior to the study, two radiologists (SK and YS) with at least 3 years' experience in abdominal imaging received instruction by an expert radiologist (KU) in reading CTC images for two days and consequently read at least 100 CTC cases. Completely blinded to the location, number, size and configuration of the LSTs in the study group, examiners initially evaluated virtual colonoscopic images and then 2-D images (primary three-dimensional search method) using a workstation (ZAIO station NG1®, ZAIO Software, Tokyo, Japan) to screen for LSTs. If two examiners made a different judgement, they discussed the results. One of the authors (KU), an experienced radiologist who was not involved in initial lesion detection, matched the lesions found on CTC and colonoscopy on the basis of an established algorithm that incorporated the location of the lesion (within one colonic segment) and its size (within 50% of its reference standard measure)[10,11].

Statistical analysis

Patient age and size of the LSTs are expressed as mean ± SD. Detection rate is expressed as a percentage (95% confidence interval). The χ^2 test or Fischer's exact test was used to analyze the detection rate by morphology, anatomical location, size category and histology. All *P* values are two-tailed. *P* values less than 0.05 were considered to indicate statistical significance. All statistical analyses were performed with the use of Intercooled

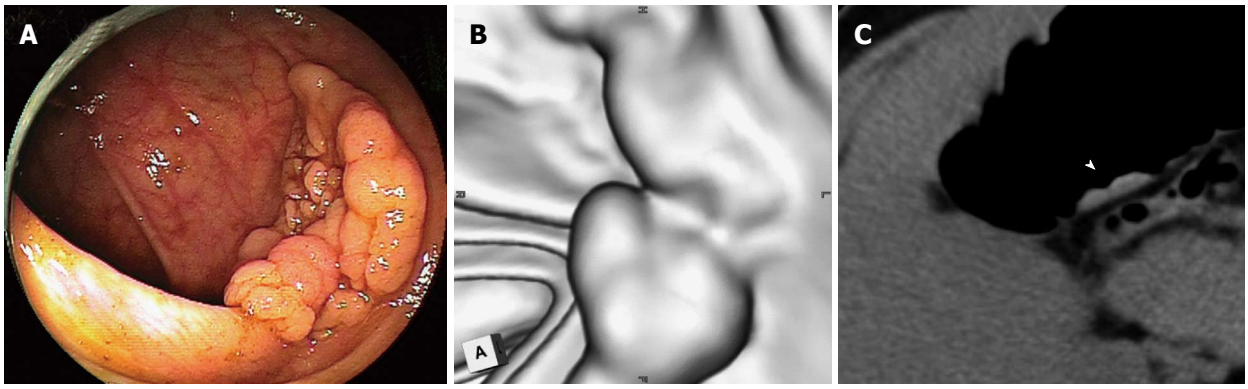

Figure 1 Thirty-six millimeter, adenoma, laterally spreading tumor, granular type. A: Optical colonoscopy image; B: Virtual colonoscopy image; C: Multiplanar reconstruction image.

Table 1 Characteristics of laterally spreading tumor reviewed prospectively *n* (%)

Morphology	Granular type	34 (72)
	Non-granular type	13 (28)
Anatomical location	Proximal colon	18 (38)
	Distal colon	19 (40)
	Rectum	10 (21)
Size	15-29 mm	24 (51)
	30-39 mm	11 (23)
	40 mm or greater	12 (26)
Histology	Adenoma	19 (40)
	Mucosal cancer (Tis)	19 (40)
	Invasive cancer (T1)	9 (19)

Stata 8.0® for Windows (Stata Corp., TX, United States).

RESULTS

Characteristics of LSTs

Two patients refused participation in the study. Eight patients were excluded from analysis because two patients did not undergo resection and six patients proved to have a cancer invading to the muscularis propria or beyond in the resected specimen. A total of 44 patients (14 women, 30 men; age 66.6 ± 8.9 years, range 42-82 years) were studied prospectively. Bowel preparation was excellent for all patients. Three patients had synchronous double LSTs. Therefore, the total number of LSTs analyzed was 47. Six LSTs for which the maximum diameter was less than 20 mm in the resected specimens (15 mm in 2, 18 mm in 2 and 19 mm in 2) were included in the analysis. Table 1 shows the morphology, anatomical location, size category and histology of the LSTs. The mean diameter of the LSTs was 35.1 ± 21.0 mm and ranged from 15 mm to 100 mm.

Comparison of virtual and optical colonoscopic images

Twenty-eight (60%) of the LSTs were correctly identified by CTC, and the configuration was similar to the colonoscopic appearance in most cases. One example is shown in Figure 1. A 36 mm lesion located in the transverse colon reveals a multi-nodular configuration on optical colonoscopy (Figure 1A), which is classified as a LST-G. The virtual colonoscopic image resembles the optical colonoscopic image although grooves on the surface are not clearly depicted on virtual colonoscopy (Figure 1B). Multiplanar reconstruction imaging depicted the lesion clearly (arrow head, Figure 1C). Histologically, the lesion is an adenoma. Another example is shown in Figure 2. A 58 mm lesion is located close to the anus on optical colonoscopy (Figure 2A). On virtual colonoscopy, however, only a part of the lesion can be identified despite its large size (Figure 2B). On axial imaging (Figure 2C), a part of the lesion was visible (arrow head), similar to the virtual colonoscopic image. Accordingly, the lesion was judged as "unable to detected by CTC". Histologically, the lesion is an adenoma. Another example is shown in Figure 3. On optical colonoscopy, this 30mm lesion is located at the bottom of the cecum. The demarcation line of the lesion is clearly depicted from the hue (Figure 3A). On virtual colonoscopy, in contrast, the lesion is unable to be detected because it is completely flat. Multiplanar reconstruction imaging was unable to depict the lesion, although the arrow-head indicates a possible location (Figure 3C). Histologically, the lesion is an adenoma.

Detection rate

Table 2 shows detection rates by morphology, anatomical location, size category (15-29 mm, 30-39 mm, 40 mm or greater) and histology. The detection rate for a LST-G was significantly higher than that for a LST-NG (71% *vs* 31%, $P = 0.020$). Correctly identified LSTs had a tendency toward a larger size, but there was no significant difference between the "30-39 mm" and "40 mm or greater" groups ($P = 0.089$). The detection rate for adenomas was significantly lower than that for mucosal cancers (32% *vs* 79%. $P = 0.008$) and T1 cancers (32% *vs* 78%, $P = 0.042$).

DISCUSSION

Advanced lesions[5] defined as adenomas or cancers measuring 1 cm or greater, containing villous components or high-grade dysplasia on histological examination are

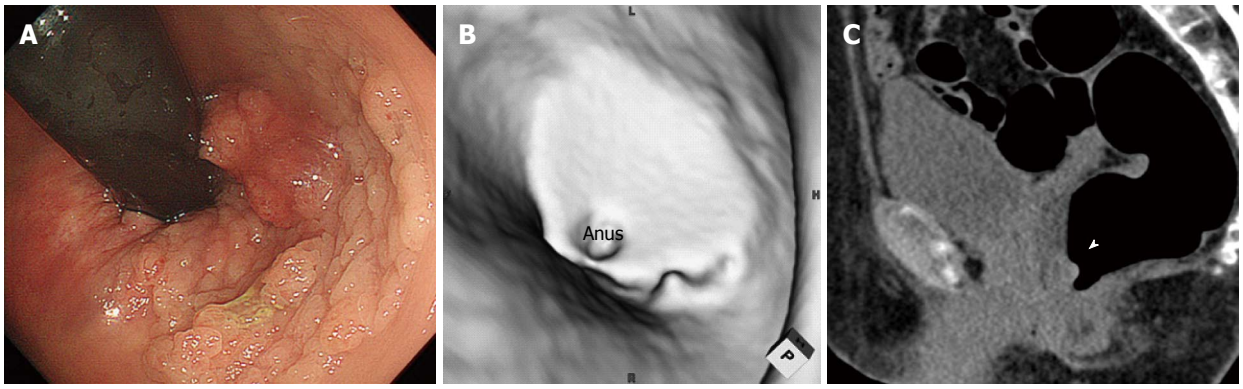

Figure 2 Fifty-eight millimeter adenoma, laterally spreading tumor, granular type, located close to the anus. A: Optical colonoscopy image; B: Virtual colonoscopy image; C: Axial image.

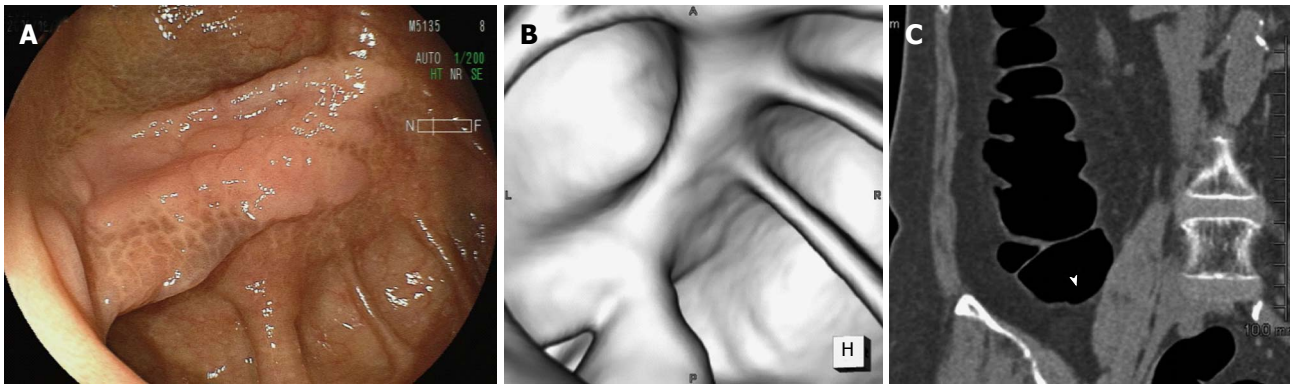

Figure 3 Thirty millimeter adenoma, laterally spreading tumor, non-granular type, located at the bottom of the cecum. A: Optical colonoscopy image; B: Virtual colonoscopy image; C: Multiplanar reconstruction image.

Table 2 Detection rates of laterally spreading tumor by morphology, anatomical location, size category and histology

		n	Detection rate (95%CI)	*P* value
Overall		47	60% (44-74)	
Morphology	Granular type	34	71% (53-85)	0.013
	Non-granular type	13	31% (9-61)	
Location	Proximal colon	18	44% (22-69)	0.250
	Distal colon	19	68% (43-87)	
	Rectum	10	70% (35-93)	
Size	15-29 mm	24	54% (33-74)	0.134
	30-39 mm	11	45% (17-77)	
	40 mm or greater	12	83% (52-98)	
Histology	Adenoma	19	32% (13-57)	0.006
	Mucosal cancer (Tis)	19	79% (54-94)	
	Invasive cancer (T1)	9	78% (40-97)	

P value is calculated by the χ^2 test.

the main targets for colon screening. According to the size criterion, LSTs are advanced lesions. In this study, LSTs measuring 20 mm or greater on colonoscopy were selected for the study group. However, the detection rate of LSTs was unsatisfactorily low to apply this technique for colon screening. In particular, the detection rate of LST-NG was approximately 30%, suggesting that LST-NG could not be detected using CTC.

Given that a flat morphology was defined as a broad-based lesion with a height of less than one half of its width[12], LST-NGs as well as LST-Gs are included as flat lesions. Flat morphology is considered one of the main causes for missed lesions evaluated by multi-detector row CTC[9]. For an expert radiologist, the detection rate of flat lesions is equivalent to that for polypoid lesions[12], but the positive predictive value for a flat lesion is lower than that for other types of colorectal lesions[13]. This implies that it is still difficult to screen for flat lesions even if the lesions are larger than 1 cm in diameter. Some authors have insisted that lesions with a height of 1 mm or less are not seen on CTC[14]. From this viewpoint, LST-NGs representing flat lesions with a very low axis cannot be identified by CTC. As shown in Figure 3, the hue rather than a slight difference in mucosal height is the key finding to identify the lesion by optical colonoscopy. This is strongly associated with a low detection rate by CTC for flat lesions.

In present study, the detection rate for both mucosal cancers and T1 cancers is nearly 80%, whereas that for adenomas is approximately 30%. A previous report using a computer-aided diagnosis system showed that the detection rate for flat T1 cancers is 83.3%[15] and that for stage Tis or T1 adenocarcinomas is 90%[16]. These facts demonstrate that most invasive LSTs can be detected by

CTC and validate CTC as an alternative to optical colonoscopy in a colon screening program.

A possible limitation of this study is the experience level of the radiologists who read the CTC images. Two novice readers received systematic education for two days and consequently read at least 100 CTC cases. According to the latest report, novice CTC readers obtained sensitivity equal to that of experienced readers after practicing an average of 164 CTC studies[17]. These data suggest that novice readers may not reach the same proficiency as an experienced reader. It is also acknowledged that there is no appropriate control group for this study. Consequently, sensitivity as well as specificity cannot be calculated based on the study data.

Bowel preparation was excellent for all patients based on the appearance during optical colonoscopy carried out before the CTC procedure where actual cleansing was used in this study instead of electric cleansing with fecal tagging. Therefore, the detection rate to identify LSTs may actually be higher than that in the standard setting of CTC. Nevertheless, the detection rate of LSTs by CTC, particularly LST-NGs, was not acceptable even with advanced lesions. Practitioners should be aware of the relatively low detection rate when using CTC to screen for these lesions.

COMMENTS

Background

Laterally spreading tumors (LSTs) are advanced lesions of the colon, thus being a major target for screening. Computed tomography colonography (CTC) is an alternative to optical colonoscopy. Polyps measuring 1 cm or greater are identified by CTC with a greater than 90% detection rate. However, it has been reported that flat adenomas can be easily missed with CTC. Since the majority of LSTs show a flat appearance, it is still unknown what percentage of LSTs can be identified with CTC.

Research frontiers

This is the first report to demonstrate that the detection rate of LSTs by CTC is relatively low. In particular, the detection rate of the non-granular type, which has an aggressive nature, is not acceptable in clinical practice.

Innovations and breakthroughs

Previous studies have reported a low detection rate of CTC for flat lesions, but no study has focused on large flat lesions measuring 2 cm or greater. This study demonstrates that CTC can miss flat neoplastic lesions regardless of their size.

Applications

Practitioners should be aware of the relatively low detection rate of LSTs by CTC, particularly LST-NGs, when using CTC to screen for these lesions. To use CTC widely for colon screening, it is imperative to develop a new method of CTC to detect such flat lesions as LSTs.

Terminology

LSTs are defined as epithelial neoplasms measuring 1 cm or greater with a low vertical axis that extends laterally along the luminal wall. Based on their endoscopic morphology, LSTs are divided into two subtypes, including LST granular type (LST-G) and LST non-granular type (LST-NG). CTC is an imaging procedure that uses a CT scanner to produce two- and three-dimensional images of the large intestine. Virtual colonoscopy, as well as an air enema image, is obtained in the three-dimensional imaging.

Peer review

The authors of this manuscript demonstrate that the detection rate of laterally spreading tumors using CTC is relatively low in prospective method. Overall, this study is interesting and valuable. In my opinion, this is priority publishing for the journal.

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