Original Article

Thai J Gastroenterol 2016
Vol. 17 No. 3
Sep. - Dec. 2016

Diagnostic Performance of Computed Tomographic Colonography using a Hospital Made Fecal Tagging Agent for Polyp Detection in Thai Adults

Srirattanapong S[1]
Leksrisawad P[1]
Pantongrag-Brown L[2]
Laothamatas J[2]

ABSTRACT

Background and Aim: Because commercial fecal tagging agents are not available in Thailand, we have prepared our own fecal tagging agent and used it for several years. The purpose of the study is to evaluate the diagnostic performance of computed tomographic colonography (CTC) using a hospital made, 30% w/v barium-based fecal tagging agent.

Materials and Methods: Our institutional review board approved this retrospective study and informed consent was waived. We assessed 70 Thai adults with colorectal polyps ≥ 6 mm detected at CTC that underwent optical colonoscopy (OC) within 6 months in Ramathibodi Hospital. Two radiologists interpreted CTCs separately and independently and were blinded to the OC results. The sensitivity of CTC was calculated on a per-polyp basis by using an OC as the reference standard. A per- patient positive predictive value using 6 mm as a threshold was also calculated. Interobserver variability for polyp detection at CTC was evaluated by calculating the Kappa inter-rater reliability.

Results: Using 6 mm as a cut-off point, overall sensitivity of CTC was 87.4%. Stratifying polyps into 6-9 mm, and ≥ 10 mm, sensitivity of CTC was 80.9%, and 93.8%, respectively. Per-patient positive predictive value was 95.7% using a 6 mm as a threshold. The K-value between 2 observers showed high to excellent agreement in identification of polyps both 6-9 mm (97.1%) and ≥10 mm (97.1%).

Conclusion: CTC using a hospital made, 30% w/v barium-based fecal tagging agent is an effective screening modality, and it could replace the commercial fecal tagging agent in our population.

Key words : Computed tomographic colonography, fecal tagging, colorectal polyps

[Thai J Gastroenterol 2016; 17(3):167-171.]

[1]*Department of Diagnostic and Therapeutic Radiology, Faculty of Medicine,* [2]*Advanced Diagnostic Imaging Center (AIMC), Ramathibodi Hospital, Bangkok 10400, Thailand.*

Address for Correspondence: *Saowanee Srirattanapong, M.D., Department of Diagnostic and Therapeutic Radiology, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok 10400, Thailand. Email: junethebest2008@gmail.com*

INTRODUCTION

Colorectal cancer is a curable disease if detected and treated early. Many screening methods have been developed to detect polyps, and some are premalignant lesions.

CT colonography (CTC), also called virtual colonoscopy, has been recently accepted as one of the screening test for colorectal cancer[1]. Data from a meta-analysis showed that the pooled per-patient sensitivity of CTC was 88% for ≥ 10 mm polyps, and 84% for 6-9 mm polyps. The pooled per-polyp sensitivity of CTC was 81% for ≥ 10 mm polyps, and 62% for 6-9 mm polyps[2]. In our previous study of the average-risk Thais[3] we found that if polyps were of medium size (6-9 mm), the chance of being neoplastic adenoma was about 67%. If polyps were of large size (≥ 10 mm), the change of being neoplastic adenomas was about 91%. In addition, a meta-analysis assessing the sensitivity of both optical colonoscopy (OC) and CTC for colorectal cancer detection revealed that CTC sensitivity is slightly higher than OC (96.1% vs. 94.7%)[4]. CTC is less invasive, and could performed faster than OC. It has very low risk of complications and does not need sedation during the study. The equipment and software are also widely available and have been improved. Therefore, CTC is a preferable and acceptable method for many patients and has been increasingly used.

Complete bowel preparation is essential for CTC to obtain accurate polyp detection because retained fecal material can mimic or obscured colonic polyp. Many different approaches have been proposed to solve this problem including cleansing technique and tagging residual fluid and feces with oral contrast agents[5-7].

Fecal tagging with barium-based oral agents are widely used to help decrease the false-positive finding of residual stool[1, 8]. By using this technique, residual feces and true polyp can be differentiated based on the difference in mean attenuation.

Although commercial fecal tagging agents, both high concentration (40% w/v) and low concentration (4.6% w/v) barium-based suspensions, are widely used, they are not available in Thailand. In our institution, we have decided to prepare our own barium-based fecal tagging and adjusted the various density of fecal tagging agents on the basis of the published results and our preliminary results. Our preliminary results showed that a 30% w/v barium-based fecal tagging agent was the best agent for differentiation between residual feces and polyps, and thereby false positive could be decreased. We have prepared our own fecal tagging agent, using a 30% w/v barium-based for several years. However, we have never evaluated the diagnostic performance of CTC using this tagging agent. We therefore, conducted this study to evaluate the diagnostic performance of CTC using a local made, 30% w/v barium-based fecal tagging agent.

MATERIALS AND METHODS

Subjects

This retrospective study was approved by our institutional review board and informed consent was waived. To identify patients, we reviewed our database of all CTC studies using a hospital-made, 30% w/v barium-based fecal tagging agent from January 2009 to December 2013.

The inclusion criterion for this study consisted of all patients with ≥ 6 mm polyps detected by CTC, of whom OC was performed within 6 months. Patients were excluded from the study if the data was incomplete, or there was a history of previous colon surgery.

Colonic preparation

All patients were instructed to have a soft, low residue/ low-fiber diet for 48 hours prior to the study. On the day before the examination, all patients took three 15-mL doses of hospital-made, 30% w/v barium-based fecal tagging agent orally after breakfast, lunch, and dinner. Three 30-mL doses of a cathartic agent, sodium phosphate (Swiff, Berlin Pharmaceuticals, Thailand) were administered, orally, at 5 PM, 7 PM, and 9 PM on the day before the examination. After midnight, there is nothing per oral, except for liquid, which was taken as necessary to prevent dehydration.

On the day of the examination, all patients were encouraged to evacuate any residual fluid and content immediately prior to the CTC examination.

MDCT technique

CTC was performed with either 64-slice MDCT (Siemens, SOMATOM Sensation 64, Siemens Medical System, Germany) or 320-slice MDCT (Toshiba, Aquilion one 320 slices, Japan). A flexible rubber catheter was inserted into the rectum. Prior to air insufflation, 10 mg of Hyoscine N-Butylbromide (The Government Pharmaceuticals Organization, Thailand) was

given intravenously to relax colon and decrease its peristalsis. The colon was, then, insufflated with room air up to individual tolerance level (approximately 40-50 puffs). The catheter was left in the rectum, and CT scout image was obtained to determine the adequacy of bowel distension by CT technologist. Additional air was insufflated into the rectum, if needed.

After air insufflation, supine CTC was performed in a cephalocaudal direction to encompass the entire colon and rectum. The patient was, then, placed in the prone position. Several additional puffs of air were administered. After a second CT scout image was obtained, the process was repeated over the same - range.

For 64-slice MDCT, parameters included 64 ± 0.6 mm section collimation, 120 kV, 0.5-second gantry rotation, 100 effective mAs in supine and 50 mAs in prone. CT images were reconstructed as 1-mm-thickness with a 0.7-mm interval.

For 320-slice MDCT, parameters included 320 ± 0.5 mm section collimation, 120 kV, 0.5-second gantry rotation, and automated tube current in supine and prone. CT images were also reconstructed as 1-mm-thickness with a 0.7-mm interval.

CTC interpretation

Both the supine and prone reconstructed image data sets were transferred to the workstation (Leonardo, Siemens Medical System, Germany; and Vitrea fX 1.1, Toshiba Medical system, Japan), where they were interpreted by two radiologists (B.L, S.S) independently. The readers were blind to the results of OC. Consensus reading or a double-read strategy, was performed if one observer found a lesion 6 mm or larger in diameter but the other did not, or if both readers found the same lesion but disagreed on size or location. A diagnosis was made after reading consensus.

Polyp size was categorized as medium size for 6-9 mm polyp and large size for ≥ 10 mm polyp. CTC study was considered having a positive result when a polyp ≥ 6 mm was detected. For a number of reasons, lesions ≤ 5 mm were not considered clinically important [8].

The data sets were analyzed using 3D endoluminal view as the primary approach. The antegrade and retrograde 3D flythrough passes were performed in both supine and prone, totaling of four passes, in order to optimize data interpretation. If polyps were detected or suspected on 3D views, 2D axial, coronal or sagittal views were used to confirm the findings and to determine the longest diameter of polyps. The location of colorectal polyps were assessed in six colonic segments (cecum, ascending colon, transverse colon, descending colon, sigmoid, and rectum), as recommended by an American Working Group on Virtual Colonoscopy[9].

Optical colonoscopy (OC)

For colonoscopic referral, we provided the endoscopists with hard copy images showing location of polyps on 3D maps, 3D endoluminal and 2D multiplanar reconstruction views.

From OC procedures, the location and size of polyps were collected using the same segmental classification scheme as CTC.

Data analysis

The results of the CTC and OC were compared and OC findings were considered as the reference standard. Results were calculated in 2 ways: individual polyp detection (per-polyp analysis) and patient detection (per-patient analysis).

Regarding per-polyp analysis, both location and size of polyps were considered for true-positive matching. Regarding the location, a polyp identified on CTC was considered concordant with one found on OC if it was located in the same or adjacent colonic segment. Regarding the size, the size measured on CTC had to be within a 50% margin of error from the size estimated on OC[6].

Regarding per-patient analysis, the overall CTC examination results were compared with the overall OC results for each patient. A case was considered true positive if CTC had detected at least one polyp seen on OC based on the location and size criteria, described previously.

Statistical analysis

Categorical variables were described by counts and percentages. Continuous variables were summarized as mean and standard deviation (SD) or median and range.

Regarding per-polyp analysis, only the sensitivity of CTC was analyzed. The specificity of CTC could not be calculated because the total number of true-negative polyps from OC could not be assessed. Regarding per-patient analysis, only the positive predictive value, and 95% CIs were calculated. Inter-observer variability of CTC per-polyp detection was evaluated by calculating the Kappa inter-rater reliability. All statistical analyses were performed using Stata V.13 (Stata Corp, College Drive, Texas, USA) statistical software.

RESULTS

The total of 70 patients were included in the study. Demographic characteristics of the study population are shown in Table 1.

OC demonstrated 95 polyps. Overall, 80 polypectomies and 15 biopsies were performed. Histologic diagnoses for matched neoplasms were as followed: hyperplastic polyp (n=39), adenomatous polyp (n=6), tubular adenoma (n=25), tubulovillous adenoma (n=8), adenocarcinoma (n=11), colonic mucosa (n=4), fibroepithelial polyp (n=1), and there was no pathological result in one case due to loss of specimen.

CTC detected 10 false positive polyps (10/95, 10.5%); 6 were ≥10 mm and 4 were 6-9 mm. Causes of false positive finding on CTC were as followed: fecal materials (n=8), mucocele (n=1), and collapsed bowel (n=1). A negative OC was observed in 3 patients.

Regarding per-polyp analysis, overall sensitivity of CTC for ≥ 6 mm polyps was 87.3% (83 of 95). Stratifying polyps into 6-9 mm, and ≥ 10 mm, sensitivity of CTC was 80.9% (38 of 47), and 93.8% (40 of 48), respectively (Table 2).

Regarding per-patient analysis, the PPV to identify patient using 6 mm as a threshold was 95.7 %.

The K-value between 2 observers showed high to excellent agreement in the identification of colorectal polyps both 6-9 mm (97.1%) and ≥ 10 mm (97.1%).

Table 1. Patients demographic data.

Number of patient	70
Age (yr)	
Mean ± SD	62.2 ± 7.5
Range	47-87
Sex	
Female: Male	37:33
Clinical history (n, %)	
• No symptom	40 (57)
• Family history of CRC	7 (10)
• With symptoms (constipation, bowel habit change, mucous bloody stool)	23 (33)

Table 2. The sensitivity on a per-polyp analysis.

Polyps	Sensitivity (%)	95% CI
≥ 6 mm (n=95)	87.4%	0.77-0.94
6-9 mm (n=47)	80.9%	0.72-0.90
≥ 10 mm (n=48)	93.8%	0.82-0.97

DISCUSSION

Our study showed that CTCs using a hospital-made 30% barium-based fecal tagging agent had high diagnostic performance in both per-polyp and per-patient analysis. Using 6 mm as a size cut-off, overall sensitivity of CTC per-polyp basis was 87.3 %. Stratifying polyps into 6-9 mm, and ≥ 10 mm, sensitivity of CTC per-polyp basis was 80.9%, and 93.8%, respectively. Regarding per-patient analysis, the PPV to identify patient using 6 mm as a threshold was 95.7%.

The sensitivity in our study were higher than the prior study in Thai population[10], which had not used a fecal tagging agent. Sensitivity of that study for ≥6 mm polyps was only 66.7% and the accuracy was 66.7%. We found that the major cause of our false positive polyps was related to fecal residues. The difference between our result and that series suggested that a local-made 30% barium-based fecal tagging agent was able to reduce the diagnostic errors related to fecal residues, resulting in increasing in sensitivity.

Many studies have evaluated the effectiveness of fecal tagging agents and optimal fecal tagging methods and showed that fecal tagging improved specificity, while sensitivity remains comparable to the non-fecal tagging group[11-13]. Yoon SH *et al.*, found that the best regimen of bowel preparation and fecal-tagging is a combination of magnesium citrate and a high concentration (40% w/v) of barium tagging agent[13]. In contrast, Kim MJ *et al.* did not demonstrate a statistically significant difference in the tagging efficacy between the use of the high and low concentration[14].

Johnson CD *et al.*, in a study with a sample size of 2,531 average-risk patients, showed that CTC sensitivity of polyps measuring 10 mm or more was 84%, per-patient sensitivity for detection of ≥ 6 mm, and ≥ 10 mm polyps was 70%, and 90%, respectively[15]. They also reported a false positive rate of 14 % for detecting polyps 10 mm or greater in diameter. Similar to our study, 10 lesions (10.5%) were falsely diagnosed with 4 lesions were 6-9 mm and 6 lesions were ≥10 mm. Although there is difference in bowel preparation, fecal tagging agent and diet, the false positive rate of our study and Johnson study was similar.

The most impressive result of our study is the high positive predictive value of CTC of 95.7%. This result means that CTC may be able to obviate the unnecessary conventional colonoscopy, which is more invasive. Moreover, closed to half of population screened by OC were found to be negative[14], which gives the CTC a good reason for an option for screening.

There were several limitations to our study. First, because of retrospectively study design, we could not perform OC in patients who had negative CTC results. Secondly, we could not perform the same-day OC in patients who had positive result on CTC. Therefore, different day OC with additional bowel preparation may possibly change location of polyps detected by CTC. However, we minimized this limitation by selection of patients whose OC was performed within 6 months of the CTC result. Third limitation was a relatively small sample size. Fourthly, we did not have a control group using other commercial fecal tagging agent. Finally, the study was conducted in a single center.

In conclusion, the high sensitivity and PPV of our CTC suggested that a hospital-made 30% barium-based fecal tagging agent could be used confidently in the bowel preparation process for CTC. For any area where commercial tagging agents is not available, one may attempt to produce a local-made, barium-based fecal tagging agent, as successfully employed in our center.

REFERENCES

1. Levin B, Lieberman DA, McFarland B, *et al.* Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps, 2008: a joint guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. Gastroenterology 2008;134:1570-95.
2. Sosna J, Morrin MM, Kruskal JB, *et al.* CT colonography of colorectal polyps: a metaanalysis. AJR Am J Roentgenol 2003;181:1593-8.
3. Pantongrag-Brown L, Pak-Art P, Patanajareet P, *et al.*. Colorectal polyps in average-risk thais: evaluation with CT colonography (Virtual Colonoscopy). Thai J Gastroenterol 2010;11:80-9.
4. Pickhardt PJ, Hassan C, Halligan S, *et al.* Colorectal cancer: CT colonography and colonoscopy for detection--systematic review and meta-analysis. Radiology. 2011;259:393-405.
5. Macari M, Lavelle M, Pedrosa I, *et al.* Effect of different bowel preparations on residual fluid at CT colonography. Radiology 2001;218:274-7.
6. Iannaccone R, Laghi A, Catalano C, *et al.* Computed tomographic colonography without cathartic preparation for the detection of colorectal polyps. Gastroenterology 2004;127: 1300-11.
7. Mahgerefteh S, Fraifeld S, Blachar A, *et al.* CT colonography with decreased purgation: balancing preparation, performance, and patient acceptance. AJR Am J Roentgenol 2009;193:1531-9.
8. Pickhardt PJ. Screening CT colonography: how I do it. AJR Am J Roentgenol 2007;189:290-8.
9. Fenlon HM, Nunes DP, Schroy PC, *et al.* A comparison of virtual and conventional colonoscopy for the detection of colorectal polyps. N Engl J Med 1999;341:1496-503.
10. Chirapitchayanawin N PW, Noola B. Accuracy of computed tomographic colonography for detection of colorectal adenoma and cancers in average-risk patients. Thai J Gastroenterol 2012;13:93-8.
11. Lefere PA, Gryspeerdt SS, Dewyspelaere J, *et al.* Dietary fecal tagging as a cleansing method before CT colonography: initial results polyp detection and patient acceptance. Radiology 2002;224:393-403.
12. Nagata K, Okawa T, Honma A, *et al.* Full-laxative versus minimum-laxative fecal-tagging CT colonography using 64-detector row CT: prospective blinded comparison of diagnostic performance, tagging quality, and patient acceptance. Acad Radiol 2009;16:780-9.
13. Yoon SH, Kim SH, Kim SG, *et al.* Comparison study of different bowel preparation regimens and different fecal-tagging agents on tagging efficacy, patients' compliance, and diagnostic performance of computed tomographic colonography: preliminary study. J Comput Assist Tomogr 2009;33:657-65.
14. Kim MJ, Park SH, Lee SS, *et al.* Efficacy of barium-based fecal tagging for CT colonography: a comparison between the use of high and low density barium suspensions in a Korean population - a preliminary study. Korean J Radiol 2009; 10:25-33.
15. Johnson CD, Chen MH, Toledano AY, *et al.* Accuracy of CT colonography for detection of large adenomas and cancers. N Engl J Med 2008;359:1207-17.