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Is there a difference between capsule endoscopy and computed tomography as a first-line study in obscure gastrointestinal bleeding?

SMALL INTESTINE

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Original Article

ABSTRACT

Background/Aims: Capsule endoscopy (CE) is currently recommended as the first-line study in the evaluation of obscure gastrointestinal bleeding (OGIB), while computed tomography (CT) is often thought of as complementary to CE. This study evaluated CT as a first-line study in OGIB and compared it with CE.

Materials and Methods: Ninety-nine patients with OGIB who received both CE and CT were included. CT included conventional CT and CT enterography (CTE). Patients were divided into two groups: the CT before CE group (CT first group; n=75) and the CE before CT group (CE first group; n=24). The two groups were compared retrospectively.

Results: Overt OGIB was present in 92% of patients. Mucosal lesions (46%) were the most common diagnoses, while tumors accounted for 7%. The diagnostic yield of CE was significantly higher than that of CT for both groups (CT first group, p<0.001; CE first group, p=0.013). In the CT first group, the diagnostic yield using both CT and CE (48/75; 64%) was significantly higher than that for CT alone (12/75; 16%, p=0.005). In the CE first group, the diagnostic yield with both CT and CE versus CE alone was 70.9% versus 62.5%, respectively, with a significant difference (p=0.045).

Conclusion: There was no significant clinical difference associated with the order in which the tests were performed. However, CE and CT, when used together, had a significantly greater diagnostic yield than did CE or CT when used alone.

Keywords: Capsule endoscopy, computed tomography, obscure gastrointestinal bleeding

INTRODUCTION

Obscure gastrointestinal bleeding (OGIB) is defined as bleeding of unknown origin that persists or recurs following a negative upper and lower endoscopy (1-3). It accounts for approximately 5%-8% of gastrointestinal (GI) bleeding cases (4,5). Although it accounts for a relatively small proportion of patients with GI bleeding, improvement in the detection rate of OGIB is needed in order to obtain a better outcome in these patients.

Of the many diagnostic modalities for the evaluation of small bowel lesions, capsule endoscopy (CE) is currently recommended as the first-line diagnostic method to evaluate patients with OGIB (6-8). However, computed tomography (CT) is easy to use, provides rapid results, and can evaluate small bowel strictures and extraluminal disease that can not be detected by CE. Because of these advantages, some consider CT as a complementary test to CE (9).

Prospective studies that compared the effectiveness of CE and conventional CT/CT enterography (CTE) in the diagnosis of patients with OGIB found that the diagnostic yield of CE was significantly higher than that of CT/CTE (57.7%-72% *vs.* 24%-30%) (10,11). However, in another prospective study that included a considerable

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number of small bowel tumors, the diagnostic yield of CTE was significantly greater than that of CE (88% *vs*. 38%) (12). Therefore, the overall evidence is inconsistent. To the best of our knowledge, the effect of the order in which diagnostic methods are performed has not yet been examined.

The purpose of this study was to evaluate the efficacy of CT as a first-line study in OGIB and to determine whether the order of diagnostic methods makes a clinical difference.

MATERIAL AND METHODS

Patients

Between March 2003 and January 2012, 554 patients underwent CE at Soonchunhyang University College of Medicine. We retrospectively analyzed records in a prospectively collected database. Of the patients, 271 (48.9%) underwent CE for OGIB. OGIB included obscure overt and obscure occult bleeding. Obscure overt bleeding was defined as clinically perceptible bleeding that recurred or persisted after a negative initial endoscopic evaluation. Obscure occult bleeding was defined as iron deficiency anemia, with or without a positive fecal occult blood test (13). Ninety-eight of 271 patients (36.1%) received both CT and CE to evaluate OGIB. Of these, one patient underwent repeat CT and CE. Thus, a total of 98 patients (99 cases) who underwent both CE and CT were enrolled. The cases were divided into two groups: patients who underwent CT prior to CE (CT first group) and those who underwent CE prior to CT (CE first group). If the symptoms were intermittent, the time interval between symptoms and the examination was measured based on the last symptom. We obtained informed consents for examinations and data collection and analysis were approved by our Ethics committee.

Capsule endoscopy procedure

Patients were examined using the PillCam™ SB/SB2 (Given Imaging, Yoqneam, Israel) or the MiroCam™ (IntroMedic Co., Seoul, Republic of Korea). CE was performed after fasting for at least 8 h and using a laxative (polyethylene glycol 2L, Colyte™, Taejun Pharmacy, Seoul, Korea) if needed. An oral defoamer (Simethicone 100 cc, Gasocol™, Taejun Pharmacy, Seoul, Korea) was administered 30 min prior to the examination. Patients undergoing CE were maintained on nil by mouth during the examination. Two hours after CE, abdominal X-ray was performed to identify gastric retention. All images were reviewed by two board-certified endoscopists. Agreement was reached on any dubious images by joint discussion.

Capsule endoscopy findings and diagnostic outcomes were further classified into five broad categories: i) vascular lesions (including angioectasia, arteriovenous malformation, varix, and Dieulafoy lesion, etc.), ii) mucosal lesions (including Crohn's disease, erythema, erosions, ulcers, etc.), iii) tumors [adenocarcinoma, lymphoma, subepithelial tumor (SET), etc.], iv) others, and v) no specific findings (14). CE findings were classified as highly relevant (P2) or less relevant (P1 or P0) lesions according to standard practice guidelines (15). A result of more than P2 was reported as only positive. The degree of cleanliness of the small bowel during CE was scored according to four categories (excellent, good, fair, or poor) (16). Finally, the quality of the images was categorized as acceptable (excellent, good, and fair) or unacceptable (poor).

Computed tomography technique

After 8 h of fasting, CT was performed. The CT categories included conventional CT and CTE with/without oral neutral enteral contrast. In conventional CT, scanning was performed using a 4- or 64-section CT system (Siemens AG, Medical Solutions, Forchheim, Germany), consisting of unenhanced, arterial, and portal venous phases. CTE was performed using a 64-section CT system, with scanning from the diaphragm to the pubis during each of the following three phases: arterial, enteric, and delayed phase. In 2007, CTE became available in our hospital. Thirty-five of 44 patients (35/44, 79.5%) underwent CTE. They were administered 1800 mL of 4.4% (weight per volume) sorbitol solution as oral neutral enteral contrast. Images were obtained from the others (9/44, 20.5%) without oral neutral enteral contrast. Iodine (140 mL) (Iomeron™, Bracco Imaging SpA, Ferentino, Italy) was injected intravenously at a rate of 4 mL/sec. CT images were evaluated by two abdominal imaging specialists using a picture archiving and communication system. CT and CE were performed within 3 months of each other. Imaging results both within and outside of the institution were included. Subsequent diagnostic studies were performed as indicated clinically.

Statistical analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) software program (SPSS 15.0; Chicago, IL, USA). All continuous variables were compared using two-tailed student's *t*-test. All categorical variables were compared using the chi-square test. Multivariate analysis was conducted using logistic regression analysis. A p value <0.05 indicated statistical significance.

RESULTS

Patient characteristics

Baseline characteristics of all patients are shown in Table 1. Of a total of 99 cases (59 males, mean age 55.7±17.0 years), the CT first group included 75 cases (mean age 55.0±17.5 years), and the CE first group included 24 cases (mean age, 57.8±15.6 years). Overt bleeding was present in more than 90% of patients in both groups (92.0% vs. 91.7%, p=0.958). No significant differences were observed between groups regarding underlying disease; previous bleeding history; drug history, such as non-steroidal anti-inflammatory drugs, anticoagulants, or antiplatelet agents; duration of symptoms; lowest hemoglobin

Table 1. Baseline characteristics of the two groups

Group	CT first	CE first	p
Cases, n (%)	75 (75.8)	24 (24.2)	
Age, mean, y	55.0	58.4	0.397
Male, n (%)	46 (61.3)	12 (50.0)	0.350
Underlying disease, n (%)	37 (49.3)	11 (45.8)	0.818
Previous bleeding history, n (%)	10 (13.3)	4 (18.2)	0.733
Drug history*	18 (24.0)	5 (20.8)	0.749
Duration of symptoms, mean, days	10.3	23.6	0.195
Lowest Hb (g/dL), mean	8.8	8.0	0.233
Transfusion unit, mean	1.38	1.65	0.604
Type of OGIB			0.958
Overt	69 (92.0)	22 (91.7)	
Occult	6 (8.0)	2 (8.0)	
Follow-up duration, mean, days	440	535	0.538

*Non-steroidal anti-inflammatory drugs/anticoagulants/antiplatelet agents
CT: computed tomography; CE: capsule endoscopy; Hb: hemoglobin; OGIB: obscure gastrointestinal bleeding

Table 2. Capsule endoscopy-related data

Group	CT first	CE first	p
Type of CE			0.596
PillCam (SB1)	26 (34.7)	10 (41.7)	
PillCam (SB2)	40 (53.3)	10 (41.7)	
MiroCam	9 (12.0)	4 (16.7)	
Interval between symptoms and CE, n (%)			0.468
<2 days	26 (38.8)	6 (28.6)	
2 days-2 weeks	27 (40.3)	8 (38.1)	
>2 weeks	14 (20.9)	7 (33.3)	
Acceptable quality of images, n (%)	68 (90.7)	19 (79.2)	0.133
Arrival at cecum, n (%)	52 (73.2)	18 (85.7)	0.239
Transit time, mean, min	417	408	0.881
Results of CE			0.826
Positive findings (P2)	42 (56.0)	15 (62.5)	
Negative findings (P1 or P0)	33 (44.0)	9 (37.5)	

CT: computed tomography; CE: capsule endoscopy

level; transfusion units; or type of OGIB. In both groups, the mean follow-up duration was over 1 year (440 and 535 days, respectively).

Capsule endoscopy and computed tomography-related data

Capsule endoscopy results are summarized in Table 2. Cases for whom the time interval between the occurrence of the last symptom and CE was less than 2 days accounted for 38.8% and 28.6% of the CT first and CE groups, respectively, but there was no significant difference between the groups. For both groups, CE was done within 2 weeks in many cases (CT first group *vs.* CE first group; 79.1 *vs.* 66.7%, p=0.468). In all cases, the CE passed through the small bowel without retention. Positive findings (P2 lesions) were higher in the CE first group than in the CT group (62.5% vs. 56.0%), but this difference was not significant (p=0.826). No difference was observed according to the sequence of studies. Mucosal ulcer/erosion was the most common finding (32.0% vs. 37.5%), followed by angiodysplasia and active bleeding (Table 3).

Conventional CT was used most frequently in both groups. Regardless of taking neutral agent, CTE was performed in 46.6% and 37.5% of patients in the CT first and CE groups, respective-

Table 3. Capsule endoscopic findings

Group	CT first	CE first
Positive findings (P2), n (%)		
Mucosal ulcer/erosion	24 (32.0)	9 (37.5)
Angiodysplasia	14 (18.7)	4 (16.7)
Active bleeding	4 (5.3)	2 (8.3)
Negative finding (P1 or P2), n (%)		
P1 lesions	10 (13.3)	2 (8.3)
Mucosal erosive lesion	9 (12.0)	2 (8.3)
Hemorrhagic spot	2 (2.7)	1 (4.2)
P0 lesions		
No findings	12 (16.0)	3 (12.5)
Poor bowel preparation	0 (0)	1 (4.2)

CT: computed tomography; CE: capsule endoscopy

Table 4. Computed tomography-related data

Group	CT first	CE first	p
Type of CT			0.727
Conventional CT	40 (53.3)	15 (62.5)	
CTE with neutral agent	28 (37.3)	7 (29.2)	
CTE without neutral agent	7 (9.3)	2 (8.3)	
Interval between symptoms and CT, n (%)			0.010
<2 days	38 (51.4)	5 (20.8)	
2 days-2 weeks	29 (39.2)	12 (50.0)	
>2 weeks	7 (9.5)	7 (29.2)	
Interval between symptoms and CT, mean, days	8.7	15.9	0.241
Interval between CE and CT, mean, days	3.6	15.0	0.033

CT: computed tomography; CE: capsule endoscopy; CTE: computed tomographic enterography

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Table 5. Computed tomography findings

Group	CT first	CE first
Positive finding, n (%)	12 (16.0)	5 (20.8)
Diagnosis-matching abnormal finding		
SB tumor	4 (5.3)	2 (8.3)
Active SB bleeding or hematoma	3 (4.0)	1 (4.1)
Mucosal lesion	3 (4.0)	0
Vascular lesion	2 (2.7)	1 (4.1)
Other	0	1 (4.1)
Negative finding, n (%)	63 (84.0)	19 (79.2)
Diagnosis-mismatching abnormal finding		
Colon mucosal lesion	3 (4.0)	2 (8.4)
Colon tumorous lesion	1 (1.3)	1 (4.1)
Vascular lesion	5 (6.7)	1 (4.1)
Other	4 (5.4)	0
Normal finding	50* (66.6)	15 (62.5)

CT: computed tomography; CE: capsule endoscopy; SB: small bowel
*One of five tumor lesions included was diagnosed as an inflammatory myofibroblastic tumor

ly. The time interval between CE and CT was significantly prolonged in the CE first group compared with the CT first group (3.6 vs. 14.4 days; p=0.036) (Table 4). CT results are summarized in Table 5.

Final diagnostic outcomes and treatment

Mucosal lesions were the most common final diagnostic outcome in the CT first and CE groups (46.7 vs. 41.7%, p=0.974), followed by vascular lesions (22.7 vs. 29.2%, p=0.814); tumors were diagnosed in only 6.7% and 8.3%, respectively. No significant differences in final diagnostic outcomes were observed between the groups.

A total of seven neoplastic lesions were detected, and all tumors were surgically resected and histopathologically confirmed. Five of the seven patients belonged to the CT first group. One patient had a confirmed inflammatory myofibroblastic tumor, and the others were diagnosed with gastrointestinal stromal tumors (GISTs). In the CE first group, the two tumors were identified as a GIST and an ectopic pancreas. CE identified active bleeding in one case, and CT diagnosed a duodenal subepithelial lesion in the other.

In both groups, most patients underwent conservative treatment, with no significant differences. More therapeutic interventions, such as endoscopy, angiography, and surgeries, were performed in the CE first group than in the CT first group (12.0% vs. 20.8%), but this difference was not significant. In the CT first group, lesions were diagnosed using CE in 37 of the 63 cases with negative findings by CT (58.7%). Of these, three cases underwent treatment.

Diagnostic yield of capsule endoscopy and computed tomography

The diagnostic yield of CT accounted for 16.0% (12/75) in the CT first group and 20.8% (5/24) in the CE first group, but the two groups did not differ significantly (p=0.585). In the CT first group, the diagnostic yield of CT was affected by the presence or absence of tumor (tumor vs. non-tumor), CT type (conventional CT vs. CTE), and transfusion units (≥3 vs. ≤2 units). In the multivariate analysis, the presence of a tumor was a statistically significant predictor (OR 21.8, 95% confidence interval 1.84-260, p=0.015).

Although there was no significant difference (p=0.575) between the two groups, the diagnostic yield of CE was 56.0% (42/75) in the CT first group and 62.5% (15/24) in the CE first group. The diagnostic yield of CE was significantly higher than that of CT in both groups (CT first group; p<0.001, CE first group; p=0.013).

The concordance rate between CT and CE was 41.7% in the CT first group and 60% in the CE first group. In the CE first group, the diagnostic yield of CTE was higher than that of conventional CT (33.3% vs. 13.3%, respectively; p=0.326). However, in the CT first group, the diagnostic yield of CTE was significantly lower than that of conventional CT (2.7% vs. 25%, respectively; p=0.029).

Diagnostic yield using both capsule endoscopy and computed tomography

In the CT first group, the diagnostic yield using both CT and CE (48/75; 64%) was significantly higher than that with CT alone (12/75; 16%, p=0.005). In the CE first group, the diagnostic yield with both CT and CE versus CE alone was 70.9% versus 62.5%, respectively, with a significant difference (p=0.045) (Table 6).

DISCUSSION

Many diagnostic modalities are used to evaluate small bowel lesions, including CE, device-assisted enteroscopy (DAE), and radiographic examinations (e.g., small bowel follow-through, enteroclysis, CTE, CT enteroclysis, CT angiography, and angiography) (17). CE, compared with DAE, has the advantages of being less uncomfortable, less invasive, and less time-consuming and providing more complete visualization of the entire small bowel (13). Compared with CT, CE allows more effective direct inspection of the small intestinal mucosa. Considering these points, CE is currently recommended as the most effective initial diagnostic method in patients with OGIB (6-8). However, the ubiquitous nature of CT, its ease of use and rapid results, as well as its more consistent diagnostic yield compared with CE favor its use as the first-line study in patients with OGIB (18).

Table 6. Diagnostic yield using both capsule endoscopy and computed tomography

		Combination (%)		Total (%)	p
		Yes	No		
First CT group: CT vs. Combination					
CT (%)	Yes	16 (12/75)	0 (0/75)	16 (12/75)	
	No	48 (36/75)	36 (27/75)	84 (63/75)	0.005
Total (%)		64 (48/75)	36 (27/75)	100 (75/75)	
First CE group: CE vs. Combination					
CE (%)	Yes	62.5 (15/24)	0 (0/24)	62.5 (15/24)	0.045
	No	8.4 (2/24)	29.1 (7/24)	37.5 (9/24)	
Total (%)		70.9 (17/24)	29.1 (7/24)	100 (24/24)	

CT: computed tomography; CE: capsule endoscopy

Particularly, for cases with suspected intestinal stricture or neoplasia, CT is recommended as the first-line diagnostic investigation (9,19).

The purpose of this study was to identify whether there was a clinical difference according to the order in which CE and CT are used. We also evaluated patient-related clinical factors that necessitate CT as the first-line study in OGIB to enhance utilization of limited medical resources, given the current situation in Korea (7).

In this study, according to the test sequence, no significant clinical difference was apparent. The diagnostic yield using both CE and CT (CT first group vs. CE first group =64.0% vs. 70.9%) and therapeutic intervention (CT first group vs. CE first group =12.0% vs. 20.8%) did not differ significantly between the two groups. In the CE first group, only two tumors were diagnosed. CT detected two tumors, one of which was diagnosed as 'active bleeding' by CE alone. Therefore, in the CE first group, the sensitivity for detecting a tumor using both CT and CE or CE alone was 100% and 50%, respectively. It would be difficult to conclude that this difference was meaningless, because few tumors were included. This may reflect a natural consequence. We believe that CT as a first-line study did not affect the diagnostic yield, because only patients who underwent both CE and CT were included in this study. In addition, lesions were discovered by CT, and DAE or surgery is performed for more cases than CE to identify the lesion site, characterize the mass, and confirm the diagnosis. Therefore, the clinical impact of CT as a first-line study could not be estimated precisely from the results of this study.

As mentioned previously, most cases (75.8%) underwent CE after CT. CT was performed first in both groups for several reasons. First, some cases were referred to us for CE, after having undergone CT in the referring hospital. If we define early and later stages as before and after 2007-which was prior to the publication of many CE guidelines-when our hospital became equipped with CTE, 34.6% of cases were early-stage data. Among them, 38% was referred to our hospital for CE, after having undergone CT in another hospital. Data after 2007 indicate that the proportion of patients in whom CT was performed in another hospital decreased to 14.2%. We believe that CTE was used as the first-line study because of its many advantages and the fact that in 2007, our hospital began using it, as it was expected to have greater sensitivity than conventional CT. In contrast to our expectations, the diagnostic yield of CTE was significantly lower than that of conventional CT in the CT first group. Although not statistically significant, we believe this finding was caused by the presence of more neoplastic lesions in the conventional CT subgroup than in the CTE group.

We also believe that physician preference, patient conditions, and financial circumstances are factors that determine CT as the first-line study. Especially in Korea, cost plays an important role in the selection of the first-line testing method, because the cost of CE is 5 times greater than that of CT or CTE. Reasons for performing CT after CE were as follows: i) for additional workup after CE was performed in another hospital, ii) recurrence or persistence of symptoms after CE, iii) for identification of the causes of active bleeding, the primary lesion of which could not be determined by CE, iv) for further workup of negative findings from CE, and v) for final diagnosis or disease characterization. One aim of this study was to identify patient-related clinical factors associated with the use of CT as the first-line study. Although the presence of tumors significantly increased the diagnostic yield of CT as the first-line study, we were not able to confirm the tumors clinically. Consequently, physicians tend to perform CT first and then decide whether CE should be performed, because it is difficult to identify the presence of a small bowel mass clinically prior to CT.

We recognize the potential limitations of this study, including its retrospective and single-center design and its relatively

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small number of patients. Because economic pressures favor the use of less expensive strategies, the two tests would not be performed routinely in the same patient; so, our study was limited to a relatively small number of patients. In addition, patient selection bias may have existed, because only patients who underwent both CE and CT were included in this study. In other words, cases of OGIB diagnosed using only CT were not included. Therefore, we do not know whether such cases can be treated using CT findings only. Therefore, only limited conclusions can be drawn about CT from our findings. In patients with OGIB, even though CT is not suitable for directly confirming the bleeding predisposition of the mucosa, it allows prior identification of minor indicator lesions of CE, as well as extraluminal lesions and the condition of blood vessels. Further evaluation using prospective, larger, and multicenter studies is needed to identify the clinical effect of CT as a first-line study. Another limitation is the heterogeneity of CT and CE examinations. With regard to CT examinations, the type of CT, method of dye injection, method of administering the contrast medium, and the type of oral contrast in this study were mixed. However, previous studies have found differences in the pharmaceuticals used as oral neutral contrast agents and their administration (11,12,20,21). In addition, although higher diagnostic yields of CE compared with CT and of CTE compared with CE have been reported, CT and CTE can not be compared directly. In addition, it is difficult to consider the difference in diagnostic yield between CT and CTE as meaningful based on the CTE study, considering that 56% of patients had small bowel tumors (12). In our study, the type of CT and whether oral neutral agents were used did not affect the diagnostic yield of CT.

In conclusion, the order in which CE and CT were performed had no statistically significant effect. However, regardless of the method sequence, the use of both CE and CT showed a significantly greater diagnostic yield than the use of either CE or CT alone. When performed together to take advantage of the strengths of each, the two diagnostic methods can complement each other well.

Ethics Committee Approval: Ethics committee approval was received for this study from the institutional review board.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

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