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FULL PAPER

Obscure gastrointestinal bleeding: diagnostic performance of 64-section multiphase CT enterography and CT angiography compared with capsule endoscopy

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Objective: To compare the diagnostic capabilities between capsule endoscopy (CE) and multislice CT (MSCT) enterography in combination with MSCT angiography for assessment of obscure gastrointestinal bleeding (OGIB).

Methods: A total of 127 patients with OGIB were looked at in this study. 82 patients (aged 42.7 ± 19.1 years; 34 males) were assigned to receive MSCT diagnosis and 67 patients to (aged 53.9 ± 16.2 years; 28 males) receive CE diagnosis. Among them, 22 patients (aged 54.1 ± 19.1 years; 12 males) received both examinations. Oral isotonic mannitol and intramuscular injection of anisodamine were performed; non-ionic contrast (iopromide, 370 mg I ml^{-1}) was intravenously administered; and then multiphase scanning was conducted at arterial, small intestinal and portal venous phases in MSCT. The results were compared with findings of reference standards including double balloon enteroscopy, digital subtraction angiography, intraoperative pathological examination and/or clinical diagnosis.

Results: Administration of anisodamine markedly increased the satisfaction rate of bowel filling (94.67% vs 28.57%; $p < 0.001$) but not the diagnostic yield ($p = 0.293$) of MSCT. Compared with MSCT, CE showed an improved overall diagnostic yield (68.66% vs 47.56%; $p = 0.010$), which was also observed in overt bleeding patients (*i.e.* patients with continued passage of visible blood) (76.19% vs 51.02%; $p = 0.013$) and in patients aged younger than 40 years of age (85% vs 51.28%; $p = 0.024$). However, CE had similar positive rates to MSCT ($p > 0.05$). Among the 22 cases in whom both examinations were conducted, CE showed no significantly different diagnostic capability compared with MSCT ($p = 0.4597$).

Conclusion: Both CE and MSCT are safe and effective diagnostic methods for OGIB.

Advances in knowledge: CE is preferred for overt bleeding or patients aged younger than 40 years. The combined use of CE and MSCT is recommended in OGIB diagnosis.

Obscure gastrointestinal bleeding (OGIB), which accounts for approximately 5% of all gastrointestinal haemorrhage cases,¹ is defined as persistent or recurring gastrointestinal bleeding without an obvious aetiology after gastroduodenoscopy and colonoscopy.^{2,3} Based on the presence or absence of clinically evident bleeding, OGIB could be divided into occult (no visible blood) and overt (continued passage of visible blood, such as haematemesis, melaena or haematochezia) bleeding.^{3,4} OGIB frequently occurs in the small bowel and is caused by small bowel diseases such as intestinal erosions, ulcers, vascular anomaly, gastrointestinal tumours and inflammatory bowel and parasitic diseases.^{5,6}

Multiple diagnostic techniques have been developed to elucidate the causes of OGIB. Among them, two non-invasive technologies, capsule endoscopy (CE) and multislice CT

(MSCT) markedly improved the ability to determine the causes of OGIB by allowing the visualization of the gastrointestinal tract.^{2,3,6} CE is able to obtain direct visualization of mucosal surface of the entire small intestine.^{4,7,8} However, capsule retention remains a major risk of CE diagnosis.^{4,9–11} In addition, the visual field restriction limits the value of CE in diagnosis of umbilicate or extraluminal lesions, since the small bowel is difficult to evaluate owing to its large length and tortuous course.^{4,10} Conversely, MSCT, including MSCT angiography (MSCTA), MSCT enteroclysis and MSCT enterography (MSCTE), has full capacity to depict the extraintestinal lesions, owing to the combination of the advantages of enteral volume challenge with the ability of cross-sectional imaging.^{4,12} Yet, substantial patient radiation exposure is one of the major disadvantages of MSCT diagnosis.^{3,13} Careful preparation is

also needed before examination.¹⁴ Considering that both CE and MSCT have advantages and disadvantages, a limited number of published data have compared the two diagnostic tools in patients with OGIB.^{4,6,15–17} However, most of these studies did not refer to MSCTA, and apparently different results were obtained owing to the advancement of the two technologies. Thus, an updated and comprehensive comparison is required.

Hence, we compared the diagnostic capability of MSCTE in combination with MSCTA with CE in patients suffering from OGIB. In this study, MSCTE and MSCTA technologies performed with a 64-slice spiral CT scanner were combined by non-contrast-enhanced scanning after oral administration of a neutral enteric contrast material (isotonic mannitol, 2.5%) and the intramuscular injection of anisodamine to restrain enterocinesia, and the following multiphase scanning at arterial, small intestinal and portal venous phases followed the intravenous infusion of non-ionic iodinated contrast material (iopromide, 370 mg I ml⁻¹). In addition, the influences of the clinical bleeding pattern and age on the diagnostic capability were also investigated.

METHODS AND MATERIALS

This study was approved by the ethics committees of the First Affiliated Hospital of Soochow University, Jiangsu, China, and the Second Affiliated Hospital of Nantong University, Jiangsu, China. Written informed consent was obtained from each study participant.

Patients

From May 2008 to September 2013, a total of 136 consecutive patients with OGIB after negative gastroduodenoscopy and colonoscopy, hospitalized in the Second Affiliated Hospital of Nantong University, were recruited in the present study. Patients who simultaneously had contraindications to iodine-enhanced MSCT (such as a history of iodine allergy, hyperthyroidism, renal insufficiency and cardiac insufficiency) and CE (such as pacemaker implantation, intestinal obstruction, luminal stenosis, diverticulum and swallowing disorders), as well as patients who could complete neither MSCT nor CE examination, were excluded from this study. According to the exclusion criteria, six patients, including one senile dementia patient who could not complete bowel filling during MSCT diagnosis and swallow the CE capsule, one patient with an implanted pacemaker owing to cardiac insufficiency, two elderly patients with severe dysphagia, one severely allergic patient and one patient with hyperthyroidism suffering from diarrhoea, were excluded. All of the enrolled patients received routine blood examination, and patients with occult bleeding received faecal occult blood testing (FOBT).

According to clinical experiences, we planned to divide 50, 50 and 30 patients into the MSCT, CE, and MSCT and CE (MSCT&CE) groups, respectively. Random grouping was performed using computer-generated random number tables generated by SPSS® v. 19.0 software (SPSS Inc., Chicago, IL). However, if patients who were allocated in the MSCT or MSCT&CE group had contraindications to iodine-enhanced MSCT or rejected to receive MSCT examination, they were re-allocated into the CE group. Similarly, if patients who were

allocated into the CE or MSCT&CE group had CE contraindications or refused CE diagnosis, they were reallocated into the MSCT group. Patients in the MSCT&CE group received CE diagnosis within 1 week after the MSCT diagnosis.

To investigate the influence of clinical bleeding pattern on the diagnosis results, patients were divided into occult and overt bleeding subgroups. Occult bleeding was defined as the presence of a positive FOBT result and/or iron deficiency anaemia, without visible haematochezia. Overt bleeding was defined as visible bleeding such as haematemesis, melaena or haematochezia.

To investigate the influence of age on the diagnosis results,¹⁰ patients were divided into 40 years of age and older and younger than 40 years of age subgroups.

Multislice CT diagnosis

Patients consumed a low fibre diet and took laxatives (50% magnesium sulphate, 100 ml) the night before the MSCT scan and were not allowed to eat before and during scanning on the examination day. MSCT examination was performed between 8:00 and 10:00 AM.

The scheme of bowel filling was discussed and performed by two radiologists (with more than 10 years' experience in imaging) according to the radiograph and/or CT film (from our hospitals or other hospitals) and the clinical features of the patients. Generally, if the radiograph and/or CT film was available and showed that no contraindications to bowel filling, such as extrinsic obstruction and perforation occurred, route I or II was selected; otherwise, non-contrast-enhanced scanning was necessary prior to bowel filling to determine the occurrence of the contraindications to ensure the safety of the examination, and, thus, route III was selected (Supplementary Figure A). In detail, a total of 1500 ml of the isotonic mannitol solution (2.5%) was orally administered to the patients prior to the non-contrast-enhanced scanning (500 ml every 15 min) (route I in Supplementary Figure A). Before the last dose was administered, the patients lay on the CT table. Then, non-contrast-enhanced scanning was performed, and bowel distention was monitored by the experienced radiologists. Satisfactory images of bowel filling were defined as the ones in which the intestinal canal with a diameter of >1.5 cm accounted for >80% of the small intestine, and the enteric contrast material successfully reached the caecum. If the image of bowel filling was not satisfactory during non-contrast-enhanced scanning, additional isotonic mannitol solution was taken before contrast-enhanced scanning (route II in Supplementary Figure A). For cases without the radiograph and CT film, the scheme of bowel filling was determined according to the result of non-contrast-enhanced scanning, and contrast-enhanced scanning was performed directly after filling (route III in Supplementary Figure A). Patients with no contraindications to anisodamine received an intramuscular injection of 20 mg of anisodamine (654-2) 10 min before the scan to minimize peristalsis and alleviate spasms.

All patients were scanned with a 64-slice spiral CT scanner (Sensation Siemens Somatom® 64; Siemens Healthcare, Erlangen, Germany). An online, real-time, anatomy-adapted, attenuation-

based current modulation technique (Care Dose 4D® 120 kV; tube current, 175 mAs; Siemens Healthcare) was used. Other parameters were collimation, 0.6 mm; pitch, 1.2; tube rotation speed, 0.5 s per rotation; smooth convolution kernel, B25f; and reconstruction interval, 3.0 mm. During the time interval of bowel filling, a indwelling venous catheter was inserted in the anterior right elbow. Just before multiphase CT scanning, the subjects received intravenous administration of iopromide (Ultravist® 370; Schering, Berlin, Germany) at a dose of 1.5 ml kg⁻¹ body weight followed by 50 ml physiological saline at a rate of 4.0–4.5 ml s⁻¹ by using an automatic power injector (Optivantage™ DH; Mallinckrodt Imaging Solutions, Hazelwood, MO). Three-phase contrast-enhanced CT scanning was performed from the dome of the diaphragm to symphysis pubis during the arterial, small intestinal¹⁸ and portal venous phases. An automatic tracking program was used to trigger the arterial phase with the region of interest placed in the abdominal aorta at the L1 vertebral body level. The arterial phase scanning was started when the aortic density reached 100 HU after injection of the iodinated contrast. The small intestinal phase scanning was conducted 15 s after arterial phase scanning, and the portal venous phase scanning was performed 20 s after small intestinal phase scanning. The data were submitted to the post workstation and picture archiving and communication systems for image processing and analysis, including multiplanar reconstruction, maximum intensity projection (MIP) and volume-rendered technique (VRT).

Images were reviewed by two independent senior doctors engaged in digestive tract disease and diagnostic imaging with more than 10 years' clinical experience. The doctors were blinded to the clinical history, results of the original reports and the results of the reference standards, including double balloon enteroscopy (DBE), digital subtraction angiography (DSA), intraoperative pathological examination and/or clinical diagnosis.

Capsule endoscopy diagnosis

Patients consumed a low fibre diet and took laxatives (50% magnesium sulphate, 100 ml) the night before the CE examination and were not allowed to eat or drink on the examination day. Patients ingested 2000–2500 ml of the isotonic mannitol solution (2.5%) within 2 h prior to the examination (600–1000 ml at the first time).

CE was performed using an OMOM capsule endoscope (Jianshan Science and Technology Group Co., Ltd, Chongqing, China) that consists four main parts: a smart capsule (13 × 27.9 mm; weight, 6 g), an image recorder jacket, a portable real-time monitor and a computer workstation. The duration of the battery of the OMOM capsule was about 8 h.¹⁹

Patients drank 50 ml of simethicone (10%) and swallowed a capsule with water 30 min later. Patients were allowed to drink a small amount of water 2 h after the capsule ingestion and to eat 2–3 h after the capsule reached the small intestine. If the capsule did not reach the pyloric canal within 60 min after swallowing, the capsule would be pushed into the small intestine using a gastroscope. During the examination, patients were allowed to move freely, but strenuous exercise and exposure to any strong

electromagnetic field were avoided. The smart capsule captured the images and transmitted them to the recorder jacket. The transit time of the capsules in the oesophagus, stomach and small intestine were recorded.

Images were reviewed and the location of lesions and pathogeny were analysed by two independent senior doctors who were engaged in digestive tract disease and endoscopic technique, with more than 10 years' clinical experience through the workstation. Both doctors were blinded to the results of the reference standards, intraoperative pathological examination and clinical diagnosis. Disagreements were resolved by discussion. The CE examinations were classified as successful if the CE reached the terminal ileum during examination or the location and pathogeny were identified although the capsule was unable to reach the terminal ileum.

Diagnosis by reference standards

The reference standards used in this study were DBE, DSA, intraoperative pathological examination and/or clinical diagnosis. Patients were diagnosed by one or several reference standards. For DBE diagnosis, a Fujinon system (Fujinon Inc, Saitama, Japan) was used, and pathogenies including parasites (such as hookworm), foreign body and ulcer could be detected. DSA diagnosis was performed by using a biplane angiography suite (Artis zee®; Siemens, Forchheim, Germany) and pathogenies including vascular malformation and tumour could be found. Tumours including cancers were mainly confirmed by pathological studies of the surgical specimens. For pathogenies that could not be diagnosed by the above methods, clinical diagnosis was performed based on the clinical data and DBE or DSA images. A definite diagnosis was made by two independent senior doctors of imaging and gastroenterology departments who had over 10 years' clinical experience. If their evaluations differed, a consensus was reached after review and discussion.

Follow-up

More than 3 months follow-up was performed for the patients in the MSCT&CE group. The clinical indexes such as re-examinations and bleeding conditions were recorded, as well as the laboratory measurements such as haematochezia and haemoglobin levels. The finding was defined as false negative if rebleeding occurred or pathogeny of OGIB was identified within 3 months.

Statistical analysis

All data were analysed with SPSS v. 19.0. The diagnostic acceptability was calculated as the number of patients who underwent MSCT or CE diagnosis divided by the number of patients who were assigned to receive the corresponding diagnosis. The true-positive rate was calculated as the true-positive results (confirmed by gold standards) divided by the positive results detected by MSCT or CE. The sensitivity, specificity, positive-predictive value, negative-predictive value and accuracy for CE and MSCT were calculated. The Fisher's exact test was used to compare the qualitative data between two groups and the satisfaction rate of bowel filling was compared between patients with and without anisodamine injection during MSCT examination. A $p < 0.05$ was considered statistically significant.

The receiver operator characteristic (ROC) curve analysis was carried out using STATA® 12.0 (StataCorp, College Station, TX).

RESULTS

Grouping and characteristics of patients

A total of 130 patients with OGIB were enrolled in this study. Patients were randomly allocated in the MSCT ($n = 50$), CE ($n = 50$) and MSCT&CE ($n = 30$) groups (Table 1). Three patients did not complete this study, including one patient in the MSCT group who was allergic to iodine and refused to receive the CE examination, one patient in the CE group who could not successfully swallow capsules and could not receive MSCT examination owing to a history of asthma, and one patient in the CE group who refused both tests. Three patients in the CE group could not receive CE examination owing to juxta-papillary duodenal diverticulum or a history of incomplete intestinal obstruction and were consequently reallocated into the MSCT group. Eight patients in the MSCT&CE group were reallocated into the MSCT group according to the grouping criteria.

Finally, 82 patients (age, 42.7 ± 19.1 years; 34 males) received MSCT diagnosis and 67 patients (age, 53.9 ± 16.2 years; 28 males) received CE diagnosis. Among them, 22 patients received both examinations (Table 1). The age and gender were not significantly different between patients who received MSCT and CE diagnoses ($p = 0.128$ and 0.968 , respectively). No statistical difference in the diagnostic acceptability between MSCT (82/83, 98.80%) and CE (67/72, 93.06%) was detected ($p = 0.065$).

Findings of multislice CT diagnosis

A total of 82 patients underwent MSCT examination. Slight body discomfort occurred in three cases (3.66%) during the administration of isotonic mannitol solution: two cases had diarrhoea, and the examination was accomplished after the symptom improved; one patient had abdominal distention, and the symptom improved by nasogastric decompression after the examination was accomplished. One patient was also hyperergic to contrast agent complicated with erythra, but the symptom improved after treatment.

Seven cases did not receive injection of anisodamine owing to suspected prostate hypertrophy ($n = 6$) and glaucoma ($n = 1$). The satisfaction rate of bowel filling in patients who received anisodamine injection was sharply increased compared with patients without anisodamine treatment (94.67% vs 28.57%; $p < 0.001$). The diagnostic yield of MSCT was also higher after

anisodamine treatment, but the difference was not significant (49.33% vs 28.57%; $p = 0.293$).

Lesions in 39 out of the 82 OGIB patients (47.56%) were successfully detected by MSCT. In 36, 1, 1 and 1 case, the lesions occurred in the small intestine (gastrointestinal stromal tumour, Figure 1), oesophagus (oesophageal varix), stomach (marginal ulcer) and colon (arteriovenous malformations, Figure 2), respectively. The pathogeny was also elucidated by MSCT, including occupying lesions in 17 cases, inflammatory lesions in 14 cases, vascular abnormalities in 4 cases, diverticulum in 2 cases and polyp in 2 cases (Table 2).

Findings of capsule endoscopy diagnosis

A total of 68 patients underwent CE examination initially. The examination could not be conducted in one case owing to adverse reactions caused by swallowing capsules. The remaining 67 cases were successfully examined with CE. Capsule retention occurred in one patient (1.47%) who was diagnosed with Crohn's disease. Capsule successfully reached the ileocaecal valve in 66 patients (97.06%). Among them, capsule was not found in the pyloric canal within 60 min after swallowing in three cases, and, thus, was pushed into the small intestine using a gastroscope. The transit times in the oesophagus, stomach and small intestine of the 63 cases were 36.3 ± 27.4 s, 42.3 ± 31.4 min and 309.4 ± 173.6 min, respectively. The capsules were successfully expelled 8–72 h after swallowing.

46 out of the 67 OGIB patients (68.66%) received positive diagnoses with CE. 89.13% of the lesions occurred in the small intestine ($n = 41$), 2.17% in the oesophagus (diverticulum) ($n = 1$), 2.17% in the stomach (polyp) ($n = 1$) and 6.52% in the colon (polyp) ($n = 3$). Among the positively diagnosed patients, 13 cases (28.26%) suffered from vascular abnormalities and 6 cases (13.04%) had mucosal inflammation. Occupying lesions, polyp and mucosal protrusion were detected in five cases, respectively. Other causes such as diverticulum, ulcer/erosion, intestinal bleeding and hookworm (Figure 3) occurred in three cases, respectively (Table 2).

Comparison of diagnostic yield between multislice CT and capsule endoscopy examinations

To investigate the influence of clinical bleeding pattern or age on the diagnosis results of MSCT and CE, the patients were divided into occult and overt bleeding subgroups or 40 years of age and older and younger than 40 years of age subgroups. Details of the detection results of pathogeny were shown in Table 2. There was

Table 1. Grouping of obscure gastrointestinal bleeding patients in the multislice CT (MSCT), the capsule endoscopy (CE) and the MSCT and CE (MSCT&CE) groups

Patients after grouping	MSCT group	CE group	MSCT&CE group	Total
Randomization grouping, n	50	50	30	130
Number of cases who did not complete this study, n	1	2	0	3
Final number of cases, n	60	45	22	127

Patients in the MSCT group received only MSCT diagnosis; patients in the CE group received only CE diagnosis; patients in the MSCT&CE group received both examinations.

Figure 1. Diagnostic images of a 53-year-old male with gastrointestinal stromal tumour, which was revealed in multislice CT as well as double balloon enteroscopy (DBE), intraoperative pathological examination and histopathological examination. (a, b) The multislice CT enterography images showed highly enhanced small bowel and hypervascular tumour (arrows). (c, d) The DBE images clearly revealed the submucosal tumour and ulcer on the surface (arrows). (e) The excised tumour (arrow). (f) Tumour cells demonstrated by haematoxylin and eosin staining.

no significant difference in the diagnostic yield of MSCT between the overt and occult bleeding subgroups (51.02% vs 42.42%; $p = 0.445$) as well as between the 40 years of age and older subgroup and the younger than 40 years of age subgroup (44.19% and 51.28%; $p = 0.521$). Similarly, the diagnostic yields of CE in the overt and occult bleeding

subgroup were 76.19% and 60% ($p = 0.109$), and those in the 40 years of age and older subgroup and younger than 40 years of age subgroup were 61.7% and 85% ($p = 0.143$), respectively.

As illustrated in Table 2, the overall diagnostic yield of CE was markedly higher than that of MSCT (68.66% vs 47.56%;

Figure 2. Diagnostic images of a 75-year-old female with arteriovenous malformation, which was revealed by multislice CT (MSCT) as well as digital subtraction angiography (DSA), intraoperative pathological examination and histopathological examination. The patient had anaemia for 2 years and showed interstitial haemorrhage of the digestive tract for 2 months. Gastroduodenoscopic and colonoscopic studies did not reveal any possible cause of chronic bleeding. (a, b) The MSCT images, which were processed using volume-rendered technique (a) and the maximum intensity projection (b) showed the enlarged artery and early opacified veins during arterial phase scanning of hepatic flexure of the colon (arrows). (c) The DSA image revealed that the mesenteric artery appeared tortuous and veins were visible too early (arrow). (d) After surgical resection, shrinkage of the malformed vascular (marked by suture) at the mucosal surface was observed. (e) Arteriovenous malformation was demonstrated by haematoxylin and eosin staining with varicose arteries and veins and no capillary vessel in the intervals.

Table 2. Comparison of diagnostic yield between multislice CT (MSCT) and capsule endoscopy (CE) examinations

Diagnosis	Pathogeny	Overall	Subgrouped by clinical bleeding pattern		Subgrouped by age	
			Overt bleeding subgroup	Occult bleeding subgroup	40 years of age and older subgroup	Younger than 40 years of age subgroup
MSCT	Total numbers of allocated patients, <i>n</i>	82	49	33	43	39
	Vascular abnormalities, <i>n</i>	4	3	1	3	1
	Occupying lesions, <i>n</i>	17	12	5	6	11
	Diverticulum, <i>n</i>	2	1	1	0	2
	Polyp, <i>n</i>	2	1	1	1	1
	Inflammatory lesions, <i>n</i>	14	8	6	9	5
	Diagnostic yield, <i>n</i> (%)	39 (47.56%)	25 (51.02%)	14 (42.42%)	19 (44.19%)	20 (51.28%)
CE	Total numbers of allocated patients, <i>n</i>	67	42	25	47	20
	Vascular abnormalities, <i>n</i>	13	11	2	10	3
	Occupying lesions, <i>n</i>	5	4	1	2	3
	Diverticulum, <i>n</i>	3	2	1	2	1
	Polyp, <i>n</i>	5	3	2	3	2
	Mucosal protrusion, <i>n</i>	5	1	4	2	3
	Mucosal inflammation, <i>n</i>	6	4	2	4	2
	Ulcer/erosion, <i>n</i>	3	2	1	2	1
	Intestinal bleeding, <i>n</i>	3	3	0	2	1
	Hookworm, <i>n</i>	3	1	2	1	2
	Diagnostic yield, <i>n</i> (%)	46 (68.66%) ^a	31 (76.19%) ^a	15 (60%)	29 (61.7%)	17 (85%) ^a

^a*p* < 0.05 compared with MSCT.

p = 0.010). For patients with overt bleeding, CE showed a notably higher yield than MSCT (76.19% vs 51.02%; *p* = 0.013). For patients with occult bleeding, no significant difference was found between CE and MSCT examinations (60% vs 42.42%; *p* = 0.244). Similar results were obtained for cases in the 40 years of age and older subgroup (61.70% for CE vs 44.10% for MSCT; *p* = 0.075). However, CE showed a significantly improved diagnostic yield in patients with OGIB in the younger than 40 years of age subgroup compared with MSCT (85% vs 51.28%; *p* = 0.024).

Comparison of positive rates between multislice CT and capsule endoscopy examinations

A total of 24 cases that were positively diagnosed by MSCT were confirmed by the gold standards including DBE, DSA, intra-operative pathological examination and/or clinical diagnosis.

The true-positive rate for MSCT was 87.50% (21/24) (Table 3). Among the 24 cases, 16 were in the overt bleeding subgroup and 8 were in the occult bleeding subgroup, and 10 in the 40 years of

age and older subgroup and 14 in the younger than 40 years of age subgroup. The true-positive rates in the overt and occult bleeding subgroups were 93.75% (15/16) and 75% (6/8), respectively (*p* = 0.249) (Table 3). Similarly, there was no significant difference in the true-positive rate between the 40 years of age and older (8/10, 80.00%) and younger than 40 years of age subgroups (13/14, 92.86%) (*p* = 0.550).

As to CE examination, 40 positively diagnosed cases were confirmed by the gold standards, including 25 patients with overt bleeding and 15 patients with occult bleeding, and 24 patients in the 40 years of age and older subgroup and 16 in the younger than 40 years of age subgroup. Overall, the true-positive rate for CE was 82.50% (33/40) (*p* = 0.731 when compared with MSCT) (Table 3). No statistical difference in the true-positive rate was detected between the overt (23/25, 92.00%) and occult bleeding subgroups (10/15, 66.67%) (*p* = 0.081) as well as between the 40 years of age and older subgroup (21/24, 87.50%) and younger than 40 years of age subgroup (12/16, 75.00%) (*p* = 0.187).

Figure 3. Diagnostic images of a 72-year-old female with hookworm infection, which was revealed by capsule endoscopy (CE) as well as clinical diagnosis and treatment. The patient visited the hospital because of palpitation for 2 months. The patient's blood showed anaemia (haemoglobin, 57 g l^{-1}). No clear aetiology of gastrointestinal bleeding was found by gastroduodenoscopy and colonoscopy. The images of CE displayed many hookworms in the enteric cavity, intestinal mucosal hyperaemia of local small intestine and a small amount of pale bloody fluid. The patient was also diagnosed as ancylostomiasis in clinical. After receiving 400 mg of albendazole treatment for 3 days in combination with iron supplement and other supportive treatments, the symptoms of the patient were alleviated.

Moreover, neither for patients with overt bleeding nor for patients with occult bleeding, there was no significant difference in the true-positive rate between MSCT and CE ($p = 1.000$ and $p = 0.001$, respectively). Also, the true-positive rate was

not significantly different between MSCT and CE for patients in the 40 years of age and older subgroup ($p = 0.597$) or younger than of age 40 years subgroups ($p = 0.165$).

Patients examined with multislice CT and capsule endoscopy

Among the 130 patients, a total of 22 cases (aged 54.1 ± 19.1 years; 12 males) were examined with MSCT and subsequently with CE. The results were confirmed by gold standards. As a result, 16 cases received positive diagnoses (72.73%), among whom 6 had tumours, 5 had inflammation, 2 had vascular abnormalities, 2 had hookworm and 2 had diverticulum (Table 4). Coincident results between CE and MSCT were obtained in 14 cases (63.63%), including 11 positive findings (10 were true positive and 1 was false positive) and 3 negative findings (2 were true negative and 1 was false negative) (Table 4). Details of the eight inconsistent findings between CE and MSCT as well as the two consistent but false findings (one false positive and one false negative) are shown in Table 4. The sensitivity, specificity, positive- and negative-predictive value and accuracy were calculated and the results are shown in Table 5. In general, CE had high sensitivity (93.75%) and low specificity (33.33%), while MSCT low sensitivity (62.50%) and high specificity (83.33%). The positive-predictive values of both CE and MSCT examinations were comparatively high (78.95% and 90.91%, respectively), as well as the negative-predictive value of CE (66.67%). The diagnostic accuracies of CE and MSCT examinations were 77.27% and 68.18%, respectively.

The diagnostic capabilities between CE and MSCT examinations were further investigated by ROC curve analysis (Figure 4). The area under curve for CE and MSCT was 0.6354 [95% confidence interval (CI), 0.4199–0.8509] and 0.7292 (95% CI, 0.5250–0.9333) ($p = 0.4597$).

DISCUSSION

In the present study, we performed a direct comparison between multiphase MSCT (MSCTE in combination with MSCTA) and CE in the diagnosis of OGIB. Although CE had an improved overall diagnostic yield compared with MSCT, no significant difference was detected in the positive rate of diagnosis. However, MSCT and CE allowed detection of different pathogenies in OGIB. Thus, they should be recommended as complementary diagnostic methods.

Both multislice CT and capsule endoscopy are safe, non-invasive and effective techniques

Careful preparations were required for MSCT scanning, including usage of laxatives and multiple contrast materials.^{20,21} These agents may lead to complications such as disordered electrolyte, nausea, vomiting, diarrhoea, stomach ache and uroschesis.^{22,23}

In our study, patients were given a laxative regime of magnesium sulphate to clean the intestinal tract, isotonic mannitol to fulfil the bowel filling and avoid disordered electrolyte, anisodamine to prevent peristalsis, and intravenous contrast agent (iopromide, 370 mg I ml^{-1}) for contrast-enhanced scanning. Only 4 out of 82 cases (4.88%) had mild complications, which may be caused by the low temperature stimulation of intestines, poor tolerance to the agent for bowel filling or slight allergy to

Table 3. Diagnostic accuracy on multislice CT (MSCT) and capsule endoscopy (CE) according to applied standards of reference

Diagnosis	Pathogeny	Overall		Subgrouped by clinical bleeding pattern				Subgrouped by age			
				Overt bleeding subgroup		Occult bleeding subgroup		40 years of age and older subgroup		Younger than 40 years of age subgroup	
		TP	FP	TP	FP	TP	FP	TP	FP	TP	FP
MSCT	Confirmed by gold standards, <i>n</i>	24		16		8		10		14	
	Vascular abnormalities, <i>n</i>	3	0	3	0	0	0	2	0	1	0
	Occupying lesions, <i>n</i>	10	1	7	0	3	1	4	1	6	0
	Diverticulum, <i>n</i>	1	1	1	0	0	1	0	0	1	1
	Polyp, <i>n</i>	1	1	0	1	1	0	0	1	1	0
	Inflammatory lesions, <i>n</i>	6	0	4	0	2	0	2	0	4	0
	Positive rate, <i>n</i> (%)	21 (87.50%)		15 (93.75%)		6 (75.00%)		8 (80.00%)		13 (92.86%)	
CE	Confirmed by gold standards, <i>n</i>	40		25		15		24		16	
	Vascular abnormalities, <i>n</i>	11	0	8	0	3	0	9	0	2	0
	Occupying lesions, <i>n</i>	5	0	2	0	3	0	2	0	3	0
	Diverticulum, <i>n</i>	2	1	1	1	1	0	1	1	1	0
	Polyp, <i>n</i>	3	1	2	1	1	0	2	0	1	1
	Mucosal protrusion, <i>n</i>	1	4	1	0	0	4	1	1	0	3
	Mucosal inflammation, <i>n</i>	3	1	2	0	1	1	1	1	2	0
	Ulcer/erosion, <i>n</i>	3	0	2	0	1	0	2	0	1	0
	Intestinal bleeding, <i>n</i>	2	0	2	0	0	0	2	0	0	0
	Hookworm, <i>n</i>	3	0	1	0	2	0	1	0	2	0
	Positive rate, <i>n</i> (%)	33 (82.50%)		23 (92.00%)		10 (66.67%)		21 (87.50%)		12 (75.00%)	

FP, false positive; TP, true positive.

contrast agent. We found that the satisfaction rate of bowel filling achieved a significantly higher level after anisodamine treatment and the diagnostic yield was consequently increased. However, change in the diagnostic yield was not statistically significant. This may be the result of small sample size in the anisodamine-treated group. Thus, further study with a large sample size is required to assess the effect of anisodamine on diagnostic yield of MSCT.

The main risk for CE examination is capsule retention with a rate of 1–3%.²⁴ Consistently, capsule retention occurred at a rate of 1.47%. The capsule was removed surgically. The mean CE transit time was 309.4 ± 173.6 min, which is slightly longer than that reported previously (265 ± 111 min).¹⁶

No serious complications were observed during both MSCT and CE examinations, suggesting that both MSCT and CE techniques described in our study were safe and effective for OGIB. However, the dose of radiation used in our study was 23.86 ± 5.03 mSv, and the risk of radiation exposure still represents a potential safety hazard in MSCT diagnosis.

Compared with capsule endoscopy, multislice CT has a limited overall diagnostic yield but a similar positive rate

Previous studies report that the diagnostic yield of MSCT varies from 24.6% to 47.6%,^{25,26} while that of CE in OGIB ranges from 38% to 83%.^{16,27–30} In this study, we reported a relatively high diagnostic yield of 47.56% and 68.66% for MSCT and CE, respectively. Despite a lower overall diagnostic yield than CE, MSCT examination in our study achieved a similar diagnostic capability to CE. However, the study power values of overall and subgroup analyses regarding positive rate were <0.75 . Hence, a multicentre study with a large sample size is required.

In addition, outcomes of CT scanning are influenced by many factors including equipment, agents and scanning mode. Compared with the previously reported positive rate of 30.08% for CT enterography,⁶ that for MSCT (87.5%) in our study was higher. The main advancement of our study contains the use of 64-slice spiral CT scanner, small intestinal phase scanning and iodine contrast agent (370 mg I ml^{-1}). Schindera et al¹⁸ demonstrated that the peak mural enhancement of normal small bowel

Table 4. Diagnostic outcomes of capsule endoscopy (CE) and multislice CT (MSCT), compared with gold standards

Cases	Gold standard			CE	MSCT
	Determination method	Pathogeny	Results		
1	Surgery	GIST	+	+	+
2	Surgery	Sarcomatoid carcinoma	+	+	+
3	DBE	CD	+	+	+
4	Surgery	Lymphoma	+	+	+
5	Surgery	GIST	+	+	+
6	DBE	CD	+	+	+
7	Surgery	Adenocarcinoma	+	+	+
8	DBE	Diverticulum	+	+	+
9	Surgery	GIST	+	+	+
10	DBE	CD	+	+	+
11	DBE	Non-specific inflammation	+	+	— ^a
12	DSA	Angiodysplasia	+	+	— ^a
13	DBE	Angiodysplasia	+	+	— ^a
14	Clinical diagnosis	Hookworm	+	+	— ^a
15	DBE	Hookworm	+	+	— ^a
16	DBE	Ulcer	+	— ^a	— ^a
17	Surgery	N	—	+	+
				Foreign body (Denture attachment)	Foreign body (Denture attachment)
18	DBE	N	—	+	—
				Mucosal protrusion (occupying lesions)	
19	Clinical diagnosis	N	—	+	—
				Mucosal protrusion (occupying lesions)	
20	DBE	N	—	+	—
				Mucosal protrusion (occupying lesions)	
21	Clinical diagnosis	N	—	—	—
22	Surgery	N	—	—	—

+, positive result; —, negative result; CD, Crohn's disease; DBE, double balloon enteroscopy; DSA, digital subtraction angiography; GIST, gastrointestinal stromal tumour; N, normal.

^aDifferent result compared with gold standards.

occurs on 13.5 ± 7.6 s after peak aortic enhancement. Thus, we added a small intestinal phase scanning 15 s after arterial phase scanning, which may provide a more effective timing for the detection of small intestinal lesions. Compared with the standard iodine concentration (300 mg I ml^{-1}), a higher iodine concentration (370 mg I ml^{-1}) increases contrast enhancement after arterial phase.^{31,32} Furthermore, MIP and VRT reconstruction techniques were used to improve the quality of CT image in this study.³³ Hence, a 64-section three-phase CT enterography combined with CT angiography employing 370 mg I ml^{-1} was recommended.

Multislice CT and capsule endoscopy have distinct value in elucidating the cause of obscure gastrointestinal bleeding

Six patients were false-negatively evaluated by MSCT. Among them, five cases were true-positively diagnosed by CE, including two cases who showed angiodysplasia, two who had hookworms and one who had inflammation at the mucosal surface. This superiority of CE may be caused by its images clearly showing the abnormalities in the surface of intestinal mucosa, vascular inflammation, ulcer, polyp and parasitic disease, as well as some cavity tumours. However, owing to the limitation of amplification

Table 5. Comparison of diagnostic capabilities between multislice CT (MSCT) and capsule endoscopy (CE) examinations in 22 cases undergoing both examinations

Parameters	CE	MSCT
True positive (n)	15	10
False positive (n)	4	1
True negative (n)	2	5
False negative (n)	1	6
Sensitivity	93.75% (15/16)	62.50% (10/16)
Specificity	33.33% (2/6)	83.33% (5/6)
Positive-predictive value	78.95% (15/19)	90.91% (10/11)
Negative-predictive value	66.67% (2/3)	45.45% (5/11)
Accuracy	77.27% (17/22)	68.18% (15/22)

ratio and visual field restriction of CE as well as the complicated structure of small intestine, full morphology of lesions could not be obtained though CE.

In addition, significant differences between MSCT and CE were also found in the overt bleeding subgroup and the younger than 40 years of age subgroup, providing a useful guideline for the selection of diagnostic method. The bleeding can be directly observed with CE, which may be the possible explanation for higher diagnostic yield in the overt bleeding subgroup. It has been reported that the main gastrointestinal lesions in young patients with OGIB are tumour, Meckel diverticulum and intestinal mucosal lesions such as Dieulafoy's lesion, Crohn's disease and Celiac disease.³ Thus, the higher diagnostic yield in the younger than 40 years of age subgroup may owing to better tolerance to CE and high proportion of intestinal mucosal lesions in young patients with OGIB. Thus, we proposed that CE is the preferred method in the diagnosis of OGIB, especially for the patients with overt bleeding and for the cases aged younger than 40 years.

False-positive diagnosis in mucosal protrusion also occurred in three cases through CE; however, the findings of MSCT

Figure 4. Diagnostic performance of capsule endoscopy (CE) and multislice CT (MSCT) examinations investigated by receiver operator characteristic (ROC) curve analysis.

were the same as the gold standards. Thus, we proposed that the mucosal protrusion detected by CE needed to be confirmed by MSCT.

CONCLUSION

According to our results, both CE and MSCT are safe, non-invasive and effective diagnostic methods for OGIB. Combination of MSCT with MSCTA improves the diagnostic ability. CE is the preferred method in the diagnosis of OGIB, especially for patients with overt bleeding and for the cases aged younger than 40 years. However, both diagnostic methods have their own advantages and disadvantages. The combined use of CE and MSCT could improve the diagnostic accuracy in OGIB patients.

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