

Original Article



Comparison of the Positive Rate and Diagnostic Value of Capsule Endoscopy and Double-Balloon Enteroscopy in Small Bowel Disease: A Retrospective Cohort Analysis

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Abstract

Background: Capsule endoscopy (CE) and double-balloon enteroscopy (DBE) have provided great help in the diagnosis and treatment of small bowel diseases (SBD). The aim of this study was to explore the positive rate and diagnostic value of CE and DBE for patients who were suspected of having SBD, and to make a comparison between the two methods.

Methods: A retrospective study was conducted to analyze the cases at Renmin Hospital of Wuhan University. We divided the patients into CE and DBE group, and recorded the basic characteristics of the patients, checking the results of CE and DBE, positive rate, sensitivity and specificity for statistical analysis.

Results: A total of 244 patients were included in our research, including 122 in the CE group and 122 in the DBE group. The positive rate of CE for intestinal diseases was 84.4%, higher than that of DBE (78.7%), but DBE (75.2% and 92.3%) had higher sensitivity and specificity than CE (70.5% and 88.2%), though the differences were not statistically significant. The three most common positive findings in patients were inflammation, erosion, or ulcers (28.7%), vascular malformations (14.3%), and eminence lesions (9.0%). CE had a higher rate detection of inflammation, erosion, or ulcers than DBE (36.1% vs 21.3%), but they both had high positive rates for vascular malformations (13.9% and 14.8%). In addition, both methods had higher positive rates in patients with gastrointestinal bleeding compared to other symptoms.

Conclusion: CE and DBE are both important methods for intestinal examination. Patients can choose appropriate tests according to their condition.

Keywords: Capsule endoscopy, Diagnosis, Double-balloon enteroscopy, Intestinal diseases, Positive rate

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Introduction

The small intestine is the longest organ in the digestive tract, and there are many types of small bowel diseases (SBD), such as infectious inflammation, erosion, ulcers, Crohn's disease, tumors, vascular diseases, etc. The small intestine is far from both ends of the digestive tract, and its special anatomical structure and location make it difficult to examine. The sensitivity and specificity of conventional checking methods are not very good, and the small intestine is a blind area for gastroscopy and colonoscopy. With the continuous development of medical technology, capsule endoscopy (CE) and double-balloon enteroscopy (DBE) have provided great help in the diagnosis and treatment of SBD.¹⁻⁴ The capsule is small in size, easy to carry, swallow and operate, and the patients are not required to be hospitalized and have no strong discomfort during use.^{5,6} DBE has the characteristics of wide field of vision and clear image, and can be used for biopsy, mucosal staining to mark the lesion site, polyps resection, foreign body removal, etc.⁷⁻⁹ However, the checking time

of DBE is long, and patients need to be checked under anesthesia; so, the risks and benefits of DBE need to be weighed comprehensively for patients with older age or many underlying diseases. The purpose of this study was to explore the diagnostic value of CE and DBE for patients who were suspected of having SBD, and to make a comparison between the two checking methods, so as to provide help in the diagnosis and treatment of SBD.

Material and Methods

Clinical Cases

From January 2016 to January 2020, we enrolled patients who underwent DBE or CE examination with informed consent at Renmin Hospital of Wuhan University. All DBE cases who met the inclusion and exclusion criteria were included, and those who were matched to the DBE group in gender and age and underwent CE were randomly selected (A total of 122 cases were randomly selected from 180 CE cases). Inclusion criteria: (1) Age over 18; (2) Patients who were suspected of SBD; (3) No

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positive results on gastroscopy and colonoscopy. Exclusion criteria: (1) Pregnant women; (2) Patients who could not tolerate the operation; (3) Patients with previous history of abdominal surgery; (4) Patients with previous history of digestive tract obstruction; (5) Patients with cardiac pacemaker or other electronic devices that may have affected the signal reception of CE; (6) Other reasons that may have caused adverse consequences. The study was reviewed by the appropriate ethics committee and was performed in accordance with the ethical standards laid down in an appropriate version of the Declaration of Helsinki (as revised in Brazil 2013). Details that might disclose the identity of the subjects in the study were omitted.

Capsule Endoscopy Examinations

Domestic OMOM capsule endoscope was approved by SFDA for clinical use in 2005, and this device was used in our study. The patients were required to have a slash-free diet one day before the checking of CE and avoid eating raw fiber food, milk, melons, fruits, etc. After fasting for 10-12 hours, the patient took compound polyethylene glycol electrolyte solution at 6 o'clock within 2 hours on the day of examination. The patients then swallowed a tiny wireless CE. In general, the capsules would pass naturally through the digestive tract of patients and take images from it, which would be then sent to sensors on the patients' chest and abdomen. The sensor is connected to a data recorder, which is attached to the patients' waist and records the data signal. After the examination, the data recorder would be removed and the data would be processed by a doctor. CE is disposable; it will pass out of the body naturally with the peristalsis of the intestine.

DBE Examinations

The equipment used in this study was DBE (EN 450P5/20/530) of Fuji company of Japan with its related accessories such as outer casing, airbag, special biopsy forceps, the attachment include snare device, injection needle, metal clip, nylon rope, German ERBE high frequency electric knife, etc. All patients were given liquid diet three days before the DBE examination, and oral compound polyethylene glycol electrolyte solution was used to clean the intestinal tract on the day before DBE examination, until slag-free water sample was excreted. All patients were evaluated by anesthesiologists and given propofol for general anesthesia during the checking of DBE. According to the patients' clinical manifestations and radiographic findings, the doctor selected the checking approach (through mouth, anus, or both). If the patient had black stool or radiographic findings were suspicious for jejunal lesions, the first choice of DBE was through the mouth, and if the patient was suspicious for ileal lesions, the first choice was the anal route. When no abnormality was found through the checking of DBE for

the first time, 5 mL methylene blue solution was injected into the submucous membrane to mark, and the DBE was entered from the other side to the marked place.

Results Interpretation and Data Collection

The CE and DBE examinations were performed by professional doctors, and the doctors were not aware of the corresponding results before the operation. After the completion of the operation, doctors made independent diagnosis combined with the clinical biopsy results and gave final conclusions after discussion. The lesions found in the video of CE or DBE were recorded as positive findings. Patients with biopsy are diagnosed based on the final pathological findings (golden standard), while other patients were diagnosed based on clinical data (combination of typical symptoms and signs, surgical history, diagnostic treatment, and final follow-up) to determine whether the patients had SBD or not, and which disease was most likely to occur.

The basic characteristics of the patients, clinical symptoms, the examination results of CE and SBE, positive rate, sensitivity and specificity were collected for analysis. The ratio of the number of cases with positive findings to the number of total cases was the positive rate. Sensitivity is the rate of finding the cause of the disease using CE and DBE in patients with SBD, and specificity is the rate of negative results in patients without SBD.

Statistical Analysis

All data was processed using SPSS 22.0 (Chicago, IL, USA). The qualitative data was analyzed by chi-square test or Fisher exact test, and the quantitative data was analyzed by two-sample *t* test. The quantitative data was expressed as mean \pm standard deviation, the confidence interval (CI) was 95%, and the significant difference was $P < 0.05$.

Results

Basic Characteristics

A total of 244 patients were included in the analysis, including 122 in the CE group and 122 in the DBE group. There were 64 males and 58 females in the CE group, with an average age of 53.59 ± 15.757 years, and 62 males and 60 females in the DBE group with an average age of 51.17 ± 13.448 years. In the CE group, obscure abdominal pain was found in 42 patients (34.4%), obscure gastrointestinal bleeding in 59 (48.4%), and other clinical symptoms (including obscure diarrhea, abdominal distension, nausea, vomit, anemia, etc) in 31 (25.4%). In the DBE group, 39 patients (32.0%) had symptoms of obscure abdominal pain, 65 patients (53.5%) had obscure gastrointestinal bleeding, and 34 patients (27.9%) had other symptoms. There was no significant difference in these basic characteristics between the two groups (see Table 1 for details).

Results of CE Examination

Among the 122 patients, ileocecal valves were reached before the batteries ran out in 106 cases; the completion rate of the whole small intestine examination was 86.9%. The average gastric and intestinal transit time were 58.2 min and 295.9 min respectively. In the CE group, 103 cases were positive; inflammation, erosion or ulcers were seen in 44 cases (36.1%), vascular malformations in 17 (13.9%), functional bowel disease in 14 (11.5%), eminence lesions in 13 (10.7%), macular tumor in 7 (5.7%), lymphatic follicular hyperplasia or lymphatic dilatation in 3 (2.5%), both Crohn's disease and polyps in 2 (1.6%), diverticulum in 1 (0.8%), and no positive findings in 19 (15.6%). The total positive detection rate was 84.4% (see Table 2 for details).

In this group, 105 patients were finally diagnosed with SBD; among them, 74 cases could be explained by the positive findings of CE, 27 cases could not be explained by the findings of CE, 4 cases had no positive findings under the CE, and the sensitivity was 70.5% (95% CI: 0.62-0.79). Seventeen patients were eventually diagnosed without SBD, of whom 15 were negative under CE and 2 were positive, with a specificity of 88.2% (95% CI: 0.71-1.05) (see Table 3). No adverse complications, such as capsule retention, capsule inhaled into the airway or incarceration in the pharyngeal muscle, occurred in the CE group.

Results of DBE Examination

Among the 122 patients in the DBE group, 96 cases had positive results, and the positive rate was 78.7%. Inflammation, erosion or ulcers were seen in 26 patients (21.3%), vascular malformations in 18 (14.8%), tumor in 15 (12.3%), eminence lesions in 9 (7.4%), Peutz-Jeghers syndrome, functional bowel disease and ordinary polyps in 6 (4.9%), Crohn's disease in 5 (4.1%), diverticulum in 3 (2.5%), macular tumor in 2 (1.6%), and no positive findings in 26 (21.3%) (see Table 2 for details).

In this group, 109 patients were finally diagnosed with SBD; among them, 82 cases could be explained by the positive findings of DBE, 13 cases could not be explained by the findings of DBE, 14 cases had no positive findings under the DBE, and the sensitivity was 75.2% (95%CI: 0.67-0.83). Thirteen patients were eventually diagnosed without SBD, of whom 12 were negative under DBE and 1 was positive, with a specificity of 92.3% (95%CI: 0.76-1.09) (see Table 3). After the checking of DBE, six patients developed abdominal pain and pharyngeal discomfort, and two patients developed pancreatitis. No bleeding, perforation or other complications occurred, and all recovered and were discharged from the hospital.

Positive Rate in Patients with Different Symptoms

In the CE group, the positive rate was 83.3% for abdominal pain, 86.4% for gastrointestinal bleeding and 83.9% for

Table 1. Analysis of Basic Characteristics of Patients in the CE and DBE Groups

Item	CE Group [N, (%)] (n = 122)	DBE Group [N, (%)] (n = 122)	χ^2 or t Value	P Value
Gender (male/female)	64/58	62/60	0.066	0.898
Age (years)	53.59 ± 15.757	51.17 ± 13.448	1.184*	0.237
Obscure abdominal pain	42 (34.4)	39 (32.0)	0.166	0.786
Obscure gastrointestinal bleeding	59 (48.4)	65 (53.5)	0.590	0.522
Other clinical symptoms	31 (25.4)	34 (27.9)	0.189	0.772

CE, capsule endoscopy; DBE, double-balloon enteroscopy.

* t value (two sample independent t test).

Table 2. Examination Results of CE and DBE in Patients with Different Clinical Symptoms

Item	CE Group [N, (%)] (n = 122)	DBE Group [N, (%)] (n = 122)	Total number [N, (%)] (n = 244)
Inflammation, erosion, or ulcers	44 (36.1)	26 (21.3)	70 (28.7)
Vascular malformation	17 (13.9)	18 (14.8)	35 (14.3)
Eminence lesions	13 (10.7)	9 (7.4)	22 (9.0)
Macular tumor	7 (5.7)	2 (1.6)	9 (3.7)
Crohn's disease	2 (1.6)	5 (4.1)	7 (2.9)
Ordinary polyps	2 (1.6)	6 (4.9)	8 (3.3)
Lymphatic follicular hyperplasia or lymphatic dilatation	3 (2.5)	0	3 (1.2)
Functional bowel disease	14 (11.5)	6 (4.9)	20 (8.2)
Tumors (lymphoma, stromal tumor, adenocarcinoma)	0	15 (12.3)	15 (6.1)
Peutz-Jeghers syndrome	0	6 (4.9)	6 (2.5)
Diverticulum	1 (0.8)	3 (2.5)	4 (1.6)
Normal	19 (15.6)	26 (21.3)	45 (18.4)
Total positive number	103 (84.4)	96 (78.7)	199 (81.6)

CE, capsule endoscopy; DBE, double-balloon enteroscopy.

Table 3. Analysis of the Positive Rate and Diagnostic Rate in the CE and DBE Groups

Item	CE Group [N, (%)] (n = 122)	DBE Group [N, (%)] (n = 122)	χ^2 Value	P Value
Obscure abdominal pain	35/42 (83.3)	29/39 (74.4)	0.982	0.416
Obscure gastrointestinal bleeding	51/59 (86.4)	56/65 (86.2)	0.002	>0.999
Other clinical symptoms	26/31 (83.9)	24/34 (70.6)	1.612	0.248
Positive rate	103/122 (84.4)	96/122 (78.7)	1.335	0.322
Sensitivity	74/105 (70.5)	82/109 (75.2)	0.612	0.434
Specificity	15/17 (88.2)	12/13 (92.3)	0.136	>0.999

CE, capsule endoscopy; DBE, double-balloon enteroscopy.

others. The positive rate in the DBE group was 74.4% for abdominal pain, 86.2% for gastrointestinal bleeding, and 70.6% for others. There was no statistical difference between the two groups (see Table 3 for details). The total positive rate of obscure gastrointestinal bleeding (86.3%) was higher than obscure abdominal pain (79.0%) and other clinical symptoms (76.9%) after combining the two checking methods (see Table 4 for details).

The most common positive findings of abdominal pain were, in decreasing order of frequency, inflammation, erosion or ulcers, functional bowel disease, Crohn's disease, vascular malformations and tumors. The main findings of gastrointestinal bleeding were, in decreasing order of frequency, inflammation, erosion or ulcers, vascular malformations, eminence lesions and tumors. The most common conditions of other symptoms were, in decreasing order of frequency, inflammation, erosion or ulcers, functional bowel disease and eminence lesions (see Table 4 for details).

Discussion

CE is a non-invasive examination with high safety and a high rate of complete checking of the small intestine, and it can visually show the lesions and directly observe the mucosa of the small intestine. In recent years, CE has also made significant progress in broader vision and

clearer images.¹⁰ But CE has some limitations: it relies on the contraction of the gut to move, the way forward is not uniform, and influenced by the anatomy of the lumen. So, there may be blind areas and omissions during the image shooting;¹¹ in addition, the cleanliness of the lumen will affect the image.¹² Most capsule endoscopes are able to photograph the ileocecal valve or colon within the working time, that is, complete the examination of the entire small intestine; however, 10% - 20% of the capsule could not reach the ileocecal valve before the battery is depleted due to various reasons. In our study, the completion rate of CE was 86.9%, which was similar to that reported in the literature.^{13,14} The mean transit time of the small intestine was 295.9 min, slightly longer than that reported in the literature.¹⁵ The positive detection rate was 84.4%, slightly higher than that reported by some researchers,¹⁶ and no adverse complications, such as capsule retention, capsule inhaled into the airway or incarceration in the pharyngeal muscle, occurred during the CE examination.

DBE is an invasive examination that can provide diagnosis, biopsy, and treatment, but it will bring a certain degree of harm to the patients. Compared with CE, DBE is more difficult and dangerous to operate and requires operators to master the technology skillfully through practice.¹⁷ The risk of missed diagnosis of distal intestinal lesions caused by incomplete intestinal examination is a

Table 4. Disease Detection Analysis of Patients with Different Symptoms

Item	Obscure Abdominal Pain [N, (%)] (n = 81)	Obscure Gastrointestinal Bleeding [N, (%)] (n = 124)	Other Clinical Symptoms [N, (%)] (n = 65)
Inflammation, erosion, or ulcers	27 (33.3)	35 (28.2)	18 (27.7)
Vascular malformation	5 (6.2)	30 (24.2)	3 (4.6)
Eminence lesions	2 (2.5)	15 (12.1)	5 (7.7)
Macular tumor	3 (3.7)	5 (4.0)	1 (1.5)
Crohn's disease	5 (6.2)	1 (0.8)	2 (3.1)
Ordinary polyps	4 (4.9)	4 (3.2)	3 (4.6)
Lymphatic follicular hyperplasia or lymphatic dilatation	0	1 (0.8)	2 (3.1)
Functional bowel disease	11 (13.6)	4 (3.2)	8 (12.3)
Tumors (lymphoma, stromal tumor, adenocarcinoma)	5 (6.2)	9 (7.3)	3 (4.6)
Peutz-Jeghers syndrome	2 (2.5)	1 (0.8)	3 (4.6)
Diverticulum	0	2 (1.6)	2 (3.1)
Normal	17 (21.0)	17 (13.7)	15 (23.1)
Total positive number	64 (79.0)	107 (86.3)	50 (76.9)

big problem. However, DBE can detect lesions missed by CE,¹⁸ so DBE should still be performed in patients with negative results of CE but still highly suspected to have small intestinal lesions. This study showed that the positive detection rate of DBE was 78.7%, higher than that of some other studies,^{7,18,19} which may be due to the more skilled and experienced operators in our hospital. After the checking of DBE, six patients developed abdominal pain and pharyngeal discomfort, and two patients developed pancreatitis, but they all recovered and were discharged.

This study showed that the positive rate of CE for intestinal diseases was higher than DBE, but the sensitivity of DBE was higher than CE, which was mainly due to the fact that some positive findings (such as erosion, ulcers, eminence lesions etc) found under the CE could not explain the etiology of the patient. In addition, the specificity of DBE was higher than CE. However, the completion of total intestinal examination by CE is relatively high, and some lesions unrelated to the etiology can be found, which is also beneficial to patients.

The three most common conditions found in patients were inflammation, erosion, or ulcers, vascular malformations, and eminence lesions. CE had a higher detection rate of inflammation, erosion, or ulcers compared to DBE, which may be due to the higher completion rate of the whole small intestine examination under CE. Both groups had high positive rates for vascular malformations, with little difference. However, some researchers showed that compared with DBE alone, the application of CE could improve the diagnostic accuracy of vasogenic intestinal bleeding, while the combination of the two could further increase the detection rate of bleeding source.¹⁸ For functional diseases of the small intestine, CE has good diagnostic value; it can be preliminarily determined whether the small intestine has a dynamic disorder or not by observing the movement of the capsule in the small intestine. CE has a higher false positive rate in the diagnosis of elevated lesions, and it is challenging to distinguish between the true submucosal mass and benign uplift caused by external compression of adjacent structures.²⁰ DBE is very valuable for tumor detection and can be used for biopsy and treatment, while CE can only roughly classify it as elevated lesion. Therefore, we believe that patients with high suspicion of malignant disease can directly choose DBE first. DBE also had a higher detection ability for Peutz-Jeghers syndrome compared to CE in our study, but some authors have suggested that if the patient has been diagnosed with this syndrome, CE can be used in later surveillance.

The European guidelines for digestive endoscopy recommend that CE should be the first-line approach for further examination of patients with gastrointestinal bleeding who are negative on gastroscopy and colonoscopy. If the results of CE are negative, conservative treatment can be given temporarily, and if rebleeding events occur, CE

can be repeated or DBE can be performed.^{21,22} For patients with obscure gastrointestinal bleeding, some studies have shown that the value of repeated CE in patients with negative CE findings for the first time is greater than that of DBE.^{23,24} ESGE recommended performing CE as soon as possible after the occurrence of hemorrhage, preferably within 14 days.²⁵ Moreover, the results of DBE are also closely related to the examination time, and emergency DBE has high diagnostic and therapeutic value.^{26,27} According to the result of our research, CE and DBE both had higher positive rate in patients with gastrointestinal bleeding compared to other symptoms, and the difference between them was small. In addition, the positive rate of CE in patients with abdominal pain and other symptoms was higher than that of DBE; thus, CE may be a suitable method in these cases. However, there was no statistical difference in the positive rate of different symptoms between the two groups, and the positive rates were both very high; thus, CE and DBE are both important methods for intestinal examination.

The limitation of this study is that the CE and DBE were not performed on the same patients. Moreover, the number of patients in our study was not very large, which requires further research to expand the sample size, and then select the most appropriate examination method for patients with different clinical symptoms.

Conclusion

CE and DBE were both important methods for intestinal examination, the positive rate of CE was higher than that of DBE, but DBE had higher sensitivity and specificity than CE. Patients can choose an appropriate test or both according to their condition.

Authors' Contribution

XY, TD, and YL conceptualized and designed the study, collaborated in data processing, collaborated in analysis. XY wrote the manuscript, YL and TD edited and critically reviewed manuscript. All authors read and approved the final manuscript.

Conflict of Interest Disclosures

The authors declare that they have no conflict of interest.

Ethical Statement

All procedures performed in this study involving human participants were in accordance with the ethical standards of institutional research committee (Renmin Hospital of Wuhan University) and with the 1964 Helsinki declaration and its later amendments.

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