A systematic review on diagnosis and treatment of gastrointestinal diseases by magnetically controlled capsule endoscopy and artificial intelligence

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Abstract

Background: Magnetically controlled capsule endoscopy (MCCE) is a non-invasive, painless, comfortable, and safe equipment to diagnose gastrointestinal diseases (GID), partially overcoming the shortcomings of conventional endoscopy and wireless capsule endoscopy (WCE). With advancements in technology, the main technical parameters of MCCE have continuously been improved, and MCCE has become more intelligent.

Objectives: The aim of this systematic review was to summarize the research progress of MCCE and artificial intelligence (AI) in the diagnosis and treatment of GID.

Data Sources and Methods: We conducted a systematic search of PubMed and EMBASE for published studies on GID detection of MCCE, physical factors related to MCCE imaging quality, the application of AI in aiding MCCE, and its additional functions. We synergistically reviewed the included studies, extracted relevant data, and made comparisons.

Results: MCCE was confirmed to have the same performance as conventional gastroscopy and WCE in detecting common GID, while it lacks research in detecting early gastric cancer (EGC). The body position and cleanliness of the gastrointestinal tract are the main factors affecting imaging quality. The applications of AI in screening intestinal diseases have been comprehensive, while in the detection of common gastric diseases such as ulcers, it has been developed. MCCE can perform some additional functions, such as observations of drug behavior in the stomach and drug damage to the gastric mucosa. Furthermore, it can be improved to perform a biopsy.

Conclusion: This comprehensive review showed that the MCCE technology has made great progress, but studies on GID detection and treatment by MCCE are in the primary stage. Further studies are required to confirm the performance of MCCE.

Keywords: detection, early gastric cancer, gastrointestinal diseases, magnetically controlled capsule endoscopy

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Introduction

Gastrointestinal diseases (GID) are common and frequently occurring diseases in the population.[1] Conventional endoscopy is the main diagnostic modality for GID. It allows gastrointestinal lesion detection and procedures such as biopsies and minimally invasive endoscopic surgeries. Conventional endoscopes or other high-level endoscopes may occasionally lead to discomfort, including nausea, vomiting, or, in rare cases, hematemesis, during examinations, which can impact patient compliance.[2] These adverse events have been reported in some instances, although their occurrence is relatively infrequent. Consequently, there is a need to explore alternative endoscopic approaches that prioritize patient comfort and tolerance. In 2006, Carpi *et al.*[2] introduced a gastrointestinal endoscopy capsule based on a magnetic shell for motion control, called magnetically controlled capsule endoscopy (MCCE). MCCE is non-invasive, painless, comfortable, and safe. It can prevent cross-infection during gastrointestinal examination and allow comprehensive observation of the gastric mucosa of large gastric cavities and small intestines, partially overcoming the shortcomings of conventional endoscopy and wireless capsule endoscopy (WCE) in diagnosing GID.[1,3] For example, WCE and traditional colonoscopy are difficult to diagnose stomach and small intestinal diseases, respectively, while MCCE can concurrently diagnose the diseases in these parts. At the same time, because of the limitations of computed tomography enteroscopy, the sensitivity of small tumors and early cancers is poor, and the cost of magnetic resonance imaging is too high to carry out large-scale screening. Therefore, MCCE is gradually being used to examine GID.

MCCE has experienced three generations of development. The first-generation MCCE system uses a handheld device for magnetic manipulation of the capsule. Representative products include the MiroCam-Navi capsule endoscopy system developed by Intromedic Ltd., South Korea[4]; OMOM Capsule Endoscopy Platform[5] developed by Jinshan, Chongqing, China; and N35 MCCE[2] designed by Alga Magneti, Italy. The first-generation MCCE systems had certain advantages, such as lower cost, but they also had limitations in terms of examination efficiency and visualization integrity. Moreover, concerns were raised regarding potential human errors leading to high rates of pathological leakage, which could result in missed diagnoses and compromised diagnostic accuracy.[2] The second-generation robotic-assisted MCCE system includes the NaviCam capsule endoscopy system developed by ANKON Technologies Co., Shanghai[6,7]; Olympus EndoCapsule system developed by a joint project of Olympus Medical Systems, Japan and Siemens Healthcare, Germany[8]; Standing-type magnetically controlled capsule endoscopy system developed by Zifu Medical Technology Co., Ltd., China[9]; and Hitron capsule endoscopy system developed by Hangzhou Huacheng Technology Co., Ltd., China[10] Compared to first-generation MCCE, second-generation MCCE provides higher image resolution and image recording speed, extended battery life, and improved ease of operation owing to the robotic arm, resulting in improved examination efficiency and visualization integrity. The third-generation MCCE system, or the robotic capsule endoscope, which originated in 2019, comprises a magnetically controlled capsule completely controlled by an automatic robot. The representative products include RC100, a fully automated MCCE system (FAMCE) developed by Jinshan Technology in Chongqing, China,[11] and Da Vinci XI, a minimally invasive surgical robot series developed by Intuitive Surgical, Inc. in Sunnyvale, California, USA.[12] Thus, the MCCE technology has been extensively developed for improved longevity, resolution, speed, and visualization.

The aim of this systematic review is to comprehensively evaluate the clinical application values of MCCE and artificial intelligence (AI) technology in GID according to its early results, report physical factors that influence the imaging quality of MCCE and other extended functions of MCCE, such as observing drug behavior in the stomach and its damage to gastric mucosa, as well as performing biopsy, etc., and promote further research and application of MCCE in screening, diagnosis, and treatment of GID. Therefore, we conducted a literature search, systematically reviewed the above contents, and gave the conclusion and the future development direction of MCCE.

Materials and methods

We conducted a systematic review of magnetic capsule endoscopy and AI for the diagnosis and treatment of gastrointestinal disorders and reported the findings in accordance with the PRISMA Collaboration Guidelines (Figure 1). The PRISMA Collaboration Guidelines are available at http://www.prisma-statement.org/.

Inclusion and exclusion criteria

Inclusion criteria were as follows: (a) about MCCE and AI technology; (b) the use of MCCE in the detection of gastrointestinal diseases; (c) the use of AI in GID; and (d) the imaging quality of MCCE as well as its extended functionality. The exclusion criteria were as follows: (a) articles

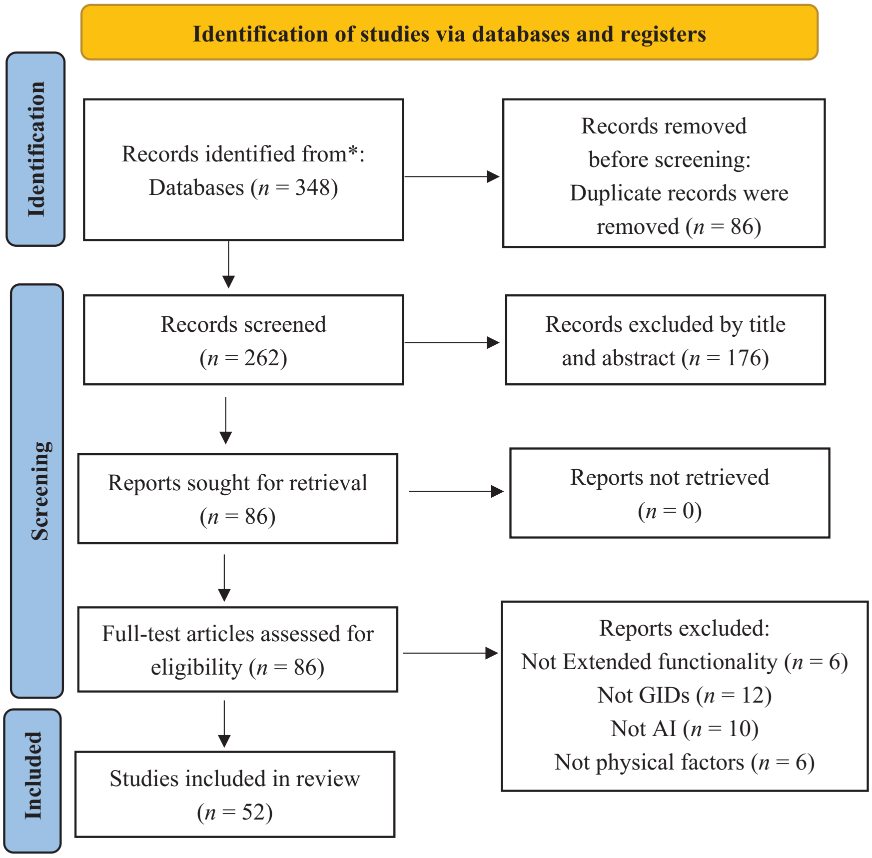

Figure 1. Flow diagram of the research method.

were not included if they did not mention the above conditions and (b) unavailable non-public literature.

Search strategy

Since November 2022, we have extensively searched electronic databases including PubMed, EMBASE, Google Scholar, Science Direct, China National Knowledge Infrastructure, Wanfang Database, etc., for potential studies and suitable articles on magnetically guided capsule endoscopy published between 2006 and 2022. The following search terms were used during the search: ('magnetically controlled capsule endoscopy' [title/abstract] or 'magnetically guided capsule endoscopy' [title/abstract] or 'capsule' [all fields]) and ('early gastric cancer (EGC)' [title/abstract] or 'GID and detection' [all fields]). fields]) AND ('Early Stage Gastric Cancer' [Title/Abstract] OR 'GID and Detection' [Title/Abstract]) AND ('overviews' [Title/Abstract] OR ('systematic review' [Title/Abstract] OR 'systematic reviews [Title/Abstract])). We then searched for other relevant articles using the reference lists of these articles. We also searched other reliable online articles, such as dissertations and book chapters, for studies that might be eligible.

Eligibility assessment and data extraction

Multiple search members independently screen the titles and abstracts of the retrieved citations and evaluate potential literature for compliance. Any disagreements that arose during the evaluation process were resolved by collective bargaining. Multiple search members were responsible for extracting the following data: the first author, year of publication, and main conclusions of each included review. During the data extraction process, the following aspects were considered and included in this paper: (1) the three generations of MCCE and their important technical parameters; (2) the ability of MCCE to detect GIDs; (3) physical factors related to the quality of the

MCCE images; (4) the applications of AI in MCCE; (5) the extended functionality of MCCE; (6) the results, discussion, and authors' recommendations; and (7) the scopes of future research and development. This systematic review analyzes relevant potential data extracted from the literature. Most of the data included only peer-reviewed journal articles.

Literature search and selection

The literature search for relevant studies from 2006 to 2022 yielded 348 study records. After removing duplicate studies, 86 records were excluded. A total of 176 records were excluded after screening by title and abstract. The remaining 86 studies were then retrieved for full-text screening and 34 studies were excluded in this step. Finally, 52 studies were included in this review. The PRISMA 2020 diagram (http://www.prisma-statement.org/) was used to show details of the literature screening process (Figure 1).

Results

Ability of MCCE to detect gastrointestinal diseases

Gastric diseases. When gastric lesions are detected using MCCE, the gastric mucosa is not as sufficiently dilated as in conventional endoscopy. The improvement of image resolution, recording speed, operational convenience due to the robotic arm, and the prolongation of battery life may bring about the improvement of overall accuracy, sensitivity, and specificity of detecting common gastric lesions from the first-generation handheld MCCE to the third-generation fully automatic MCCE. For example, Liao *et al.*[7] obtained overall sensitivity and specificity of 90.4% and 94.7%, respectively, in 353 patients using the second-generation system NaviCam for detecting gastric polyps and erosions. The overall sensitivity and specificity of the third-generation automatic system RC100 for detecting common gastric lesions (e.g. gastritis, polyps, submucosal protuberances, mucosal erosion, and xanthoma) have reached 97.44% and 99.70%, respectively.[11] These findings indicate a high clinical value of MCCE in detecting common gastric lesions.[13] Figure 2 summarizes the types of gastric lesions detected by MCCE in recent years and the number of corresponding studies, with references and other information, are shown in Table 1.

The included studies above were primarily retrospective, case series, and pilot studies. It is worth noting that gastric polyps, gastritis, gastric erosion, and ulcers were frequently reported in the existing studies, which is consistent with their prevalence among patients. However, the occurrence of precancerous lesions, gastric tumors, and

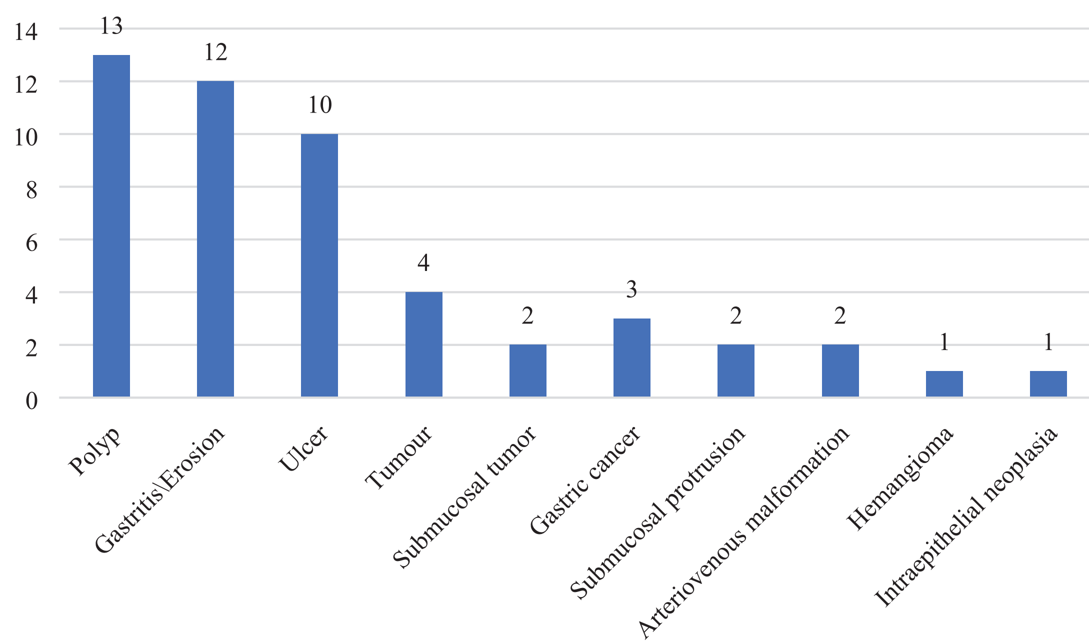

Figure 2. Gastric lesions examined by MCCE and the number of corresponding studies.
MCCE, magnetically controlled capsule endoscopy.

Table 1. The reference and other information of each study are in Figure 2.

Study	Gastric lesions (m^a/n^b)	Overall sensitivity
Rahman *et al.*[14]	Erosion (4/26), gastritis (4/26)	\
Lien *et al.*[15]	Polyp (1/9)	\
Liao *et al.*[16]	Polyp (1/34), erosion (6/34)	\
Gu *et al.*[6]	Gastritis (66/129), polyp (2/129), ulcer (1/129)	\
Jiang *et al.*[17]	Gastritis (24/40), polyp (6/40), ulcer (3/40), submucosal protrusion (1/40), arteriovenous malformation (1/40), gastric cancer (1/40)	\
Wang *et al.*[18]	Gastritis (4/9), erosion (3/9), ulcer (2/9)	\
Qian *et al.*[19]	Erosion (1/60), polyp (6/60), ulcer (2/60)	\
Zhu *et al.*[20]	Gastritis/erosion (21/158), polyp (27/158), ulcer (21/158)	\
Wang *et al.*[21]	Gastritis (7/83), fundus varices (1/83), polyp (8/83), ulcer (4/83), gastric cancer (1/83)	\
Rey *et al.*[8]	Gastritis/erosion (10/61), polyp (11/61), ulcer (5/61), angioma (1/61), metaplasia (1/61), bleeding (2/61)	\
Lai *et al.*[9]	Erosion (5/161), polyp (1/161), ulcer (1/161)	\
Liao *et al.*[7]	Polyp, ulcer, submucosal tumor, early gastric cancer, xanthoma, diverticulum, varicosity	90.4%
Zhao *et al.*[22]	Gastric cancer (7/3182), ulcer (145/3182), polyp (319/3182), submucosal tumor (114/3182)	\
Qian *et al.*[23]	Gastric cancer	91.7%
Gao *et al.*[24]	Erosion/ulcer (13/68)	\
Chen *et al.*[25]	Ulcer (3/26)	\
Lai *et al.*[26]	Ulcer (83/580), polyp (90/580)	\
Xiao *et al.*[11]	Gastritis, erosion, xanthoma, submucosal protrusion, polyp	97.44%

[a]*n* Indicates the number of subjects.
[b]*m* Denotes the number of subjects with corresponding gastric lesions detected.

gastric cancer was relatively rare in the studies analyzed (Figure 2 and Table 1). Among them, most of the gastric preparation techniques were performed according to the guidelines for bowel preparation before examination.[6–9]

Studies on the detection of gastric tumors and cancer using MCCE were mainly based on the small sample size. Jiang *et al.*[17] found gastric cancer only in 1 of 80 subjects using the second-generation system NaviCam. Zhao *et al.*[22] found gastric cancer in only seven patients and gastric submucosal tumors in only 114 patients. The samples collected by Qian *et al.*[23] are 10 patients with superficial gastric tumors. Due to insufficient samples of gastric tumors or cancer in existing studies, the specificity and sensitivity of MCCE for detecting them could not be reliably demonstrated. Gastric cancer is a malignancy with a high mortality rate. If detected at an early stage, the survival rate of patients can reach 90%.[1] However, no study has detected EGC using MCCE, implying that the detection of gastric tumors, EGC, and advanced gastric cancer using MCCE should be vigorously studied in the future for obtaining more robust conclusions.

Intestinal diseases. MCCE has become the mainstream diagnostic method for intestinal diseases.[27] The reason is that computed tomography enteroscopy has its limitations, such as the need to inject contrast agents, radiation, and poor sensitivity to small tumors and early cancers; Magnetic resonance enterography is a promising alternative method, but its cost is too high to carry out large-scale screening; Compared with the following contraindications, MCCE allows patients to identify the lesion area more acceptably, especially for occult intestinal bleeding, Crohn's disease of small intestine and small intestinal tumors. Zhang *et al.*[25] conducted a MCCE experiment for 52 people. The median intestinal transit time was 240 min, the median capsule excretion time was 24 h, and the excretion rate was 100%. 94.2% of people were completely tolerant of MCCE. Traditionally, the small intestine is generally examined by WCE or capsule endoscopy. For MCCE, after the examination of the upper digestive tract, the doctor will allow MCCE to be removed from the body after the small intestine peristalsis. In this process, MCCE, like traditional WCE or capsule endoscopy, takes pictures of the lesions in the small intestine while passing through the small intestine.

However, in our search process, there are few literature using MCCE to examine small intestinal lesions. There are only three articles[24,25,28] on the study of gastrointestinal injury caused by drugs such as aspirin. At the same time, a document[6] detected the effect of applying MCCE to GID in children, including lymphatic follicles and ulcers on terminal ileum, celiac disease, blue rubber bleb nevus syndrome, and polyps.

In the study,[17] the author proposed that the completion rate of capsule endoscopy in the small intestine examination was 83.5%, while the completion rate of MCCE could reach 100% by virtue of its magnetic steering. This suggests that MCCE may have a more reliable role in small intestine examination. This requires future researchers to carry out comparative experiments between MCCE and WCE in the integrity of small intestine examination and the detection rate of lesions.

Physical factors related to imaging quality of MCCE

Gastric imaging. Gastric anatomical landmarks are very important location indicators for the treatment of gastric diseases. The rates of gastric landmarks' visualization can be improved by changing the body positions (e.g. left lateral, supine, right lateral, knee–chest, and setting) during gastroscopy[19]; it is also related to gastric preparation protocols before the examination (such as cleaning and dilation of the stomach), and a clean and well-prepared stomach can shorten the time of gastroscopy.[20]

The influence of body positions. During gastroscopy, changes in body position can affect the imaging quality of MCCE at various anatomical landmarks. Wang *et al.*[21] observed the imaging quality of gastric landmarks in different positions and obtained the following results: the visualization of the cardia and body was the highest in the supine; the left lateral was the best position for visualization of the fundus; right lateral and sitting positions was the best for antrum observation; for the angle that is difficult to observe, the capsule can be moved to the angle under the influence of the knee–chest position and gravity to realize the movement observation of the angle and the visualization of the mucosa; in the sitting position, the capsule can reach the bottom of the maxillary sinus, and then change the position to the right lateral, the maxillary sinus and pylorus can be observed.[19] Therefore, different body positions have different imaging effects on various gastric landmarks, but only one body position cannot fully visualize all gastric landmarks well.

Wang, *et al.* further observed the effect of the combination of multiple positions (left lateral + supine + right lateral) and other combinations on the imaging quality of the stomach.[19] They found that the combination of multiple positions can improve the imaging quality of the stomach. The study also found that drinking enough water to distend the stomach and subject the subjects to changes in body position resulted in better capsule navigation and better mucosal visualization.

The effect of stomach cleaning. During gastroscopy, gastric mucus, air bubbles, and other residues will not only affect the imaging of gastric mucosa but also affect the accuracy of its diagnosis. Antifoams can prevent the formation of air bubbles in the stomach by reducing the surface tension of the air bubbles and destroying them. Pronase can cleave the peptide bonds of proteins and has a strong proteolytic effect. Therefore, in routine MCCE, these substances can reduce the amount of mucus and air bubbles and improve the diagnosis of gastric lesions. Tang *et al.*[20] observed the effect of different combinations of simethicone (antifoam), water, and pronase on MCCE imaging quality and concluded that swallowing simethicone with water prior to MCCE examination yielded the best visualization of gastric mucosa while adding pronase did not bring about a significant improvement, and the imaging quality after gastric cleaning was significantly better than that without gastric cleaning.

Holwerda *et al.* have shown that gravity affects all organ systems in the body, intra-gastric content distribution depends on posture and different body position changes can prolong the exposure time of gastric mucus to the drug.[29] The stomach is affected by gravity and empties low-nutrient fluids. Studies have shown that gastric emptying was faster in the upright position compared to lying down.[28,30,31] In an earlier study, the patients were asked to perform repeated position changes 15 min before the MCCE examination, which ensures the distribution of the cleaning agent throughout the gastric cavity and prolongs its exposure time.[21] These measures will increase the effectiveness of the cleaning agent and improve the imaging quality of MCCE. Due to the special structure of the stomach, the deep mucosal folds of the greater curvature render mucus and bubbles relatively inaccessible to dimethicone. Under the influence of gastric peristalsis and gravity, the contact time of the proximal mucosa detergent is reduced. Therefore, the cleanliness of the proximal stomach (cardia, fundus) is worse than that of the distal stomach (antrum, pylorus), and the imaging quality of the distal stomach is better than that of the proximal stomach.[20]

Intestinal imaging. The intestine is a long and complex digestive tube that runs from the pylorus to the anus and so the capsule has a long retention time in the intestine. Air bubbles, mucus, bile, and food substances in the intestine can reduce the visualization of the intestine during capsule endoscopy. Due to delayed gastric emptying, the visualization of the intestine becomes incomplete if the capsule remains in the same part of the stomach or intestine for more than 4 h, resulting in poorer image quality.[32]

Polyethylene glycol (PEG) is the most commonly used intestinal cleanser in capsule endoscopy.[33] Other cleansers include magnesium citrate and Gatorade's Miralax (polyethylene glycol 3350). Song *et al.*[34] performed multiple randomized controlled trials with or without polyethylene glycol, using different doses, and under fasting and bowel cleansing, which showed that PEG solution enhanced the visualization quality of the small intestine but did not contribute to the visual integrity of the cecum and that bowel preparation with fasting or administration of PEG solution combined with dimethicone oil enhanced visualization. Thus, bowel cleansing prior to MCCE would help to improve the imaging quality of the images.

Excessive small bowel peristalsis or rapid transit can result in incomplete small bowel assessment or missed small bowel lesions, and imaging quality at some sites such as the proximal duodenum and jejunum can become poor.[35] Kim *et al.*[36] found that bile worsened fluid transparency as the capsule advanced through the intestine and that coffee enemas resulted in bile duct dilation and bile excretion through the colonic wall. Compared to patients who received only PEG, patients who received the combination of coffee enema and 2L PEG showed greater cleanliness in the distal intestine, and coffee enema improved bile-induced visual impairment in distal small bowel images, but there was no significant change in proximal cleanliness, so the quality of visualization of the proximal small bowel remains to be improved.

In addition, gender and small bowel transport time can also affect the image quality of capsule endoscopy. Ponte *et al.*[37] evaluated the predictors of incomplete bowel examination and inadequate cleanliness in capsule endoscopy and showed that the male gender tends to imply more complications such as celiac disease, ulceration, and bleeding, which often lead to bowel complexity and thus affect the imaging quality, while increased bowel transport time can prevent the capsule from reaching the cecum in a timely manner, thus reducing the observed integrity of the bowel and increasing the probability of complications.

Applications of AI in aided diagnosis of GID

Considering that MCCE images are produced at a speed of five frames/s, approximately 6000 ($5 \times 20 \times 60$) images would be obtained for a gastric examination of 20 min. The capsule endoscope enters the stomach from the esophagus and then into the intestine. The whole process takes about 6–6h, and generates about 50,000–60,000 photos during this process.[13] Xia *et al.*[38] studied 1,023,955 MCCE images of 797 patients, with approximately 28% invalid images, and found that approximately 67% of images were of normal mucosa while only 5% images contained lesions. If all images produced by MCCE in a gastric examination are sent to doctors for screening, the workload for the doctors would be heavy. A large number of images may result in misdiagnosis or missed diagnosis because of fatigue and other subjective issues arising from reading a large number of MCCE images for a long duration by doctors. In recent years, several studies have shown that an automatic image interpretation system based on AI technology could improve the diagnostic accuracy and efficiency of MCCE.[39] At present, the applications of AI in MCCE mainly include lesion detection such as vascular diseases (gastrointestinal bleeding, vasodilatation), inflammatory diseases (ulcers and erosions), and precancerous lesions, polyp localization, and cleaning quality assessment.[40–42]

Gastric diseases. Xia *et al.*[38] developed a novel automatic gastric lesion detection system that could identify five common lesions (erosions, polyps, ulcers, submucosal tumors, and xanthogranuloma) with a sensitivity of 96.2% and a specificity of 76.2%. In terms of image processing speed, the processing time of the system per image was 44msec per image, compared to 0.38 ± 0.29 s per image for clinicians; thus, the system greatly reduces diagnostic time and improves diagnostic accuracy. Pan *et al.*[43] developed a real-time diagnostic system [Smart Data Service System-AI (sdss-AI)] for the detection of gastric lesions and anatomy. The overall sensitivity of sdss-AI for detecting gastric lesions was 98.9%, 94.2%, and the overall accuracy of identifying gastric anatomical landmarks (cardia, fundus, body, greater curvature, lesser curvature, vessels, sinus, and pylorus) with a processing time of 94.2ms per image The study showed that sdss-AI can be used for real-time diagnosis and localization of gastric lesions in magnetron capsule endoscopy, which will help physicians to improve the level of lesion detection.

Intestinal diseases. Ding *et al.*[44] achieved a sensitivity and specificity of 99.9% and 99.9%, respectively, using AI-assisted film reading. Compared with the traditional film reading, the sensitivity and specificity were increased to 25.3% and 23%, respectively. In terms of reading time, AI-assisted reading was 5.9min, about 6% of the 96.6min of manual reading. Hwang *et al.*[45] used 7556 images containing hemorrhagic and ulcerative lesions to train the AI algorithm and obtained 96.83% accuracy of lesion detection and 97.60% sensitivity on the test set.

In addition, Nam *et al.*[46] automatically calculated small bowel (SB) cleaning scores on 400,000 capsule endoscopy images using simple deep learning methods, and the Top-1 accuracy was as high as 93% for the intestinal cleaning quality assessment. In terms of reducing film reading time, Al-shebani *et al.*[47] proposed a frame reduction system based on color structure similarity, which achieved a frame reduction rate of 93.8%. Various manufacturers of MCCE have also designed software platforms using AI technology, such as Omni Mode (Endocap, Olympius, Tokyo, Japan),[48] Express View (MiroCam, IntroMedic, Seoul, South Korea),[49] and so on.

In summary, the applications of AI in screening intestinal diseases have been comprehensive, while the application for stomach screening has been developed in the detection of common gastric diseases such as ulcers. So far, there is no report about AI-aided detection and segmentation of ECG or advanced gastric cancer and so it is the direction of future efforts.

Other functions of MCCE

For gastric diseases. MCCE can be used to visualize drug behavior in the stomach and drug damage to the gastric mucosa. Wang *et al.*[18] used NaviCam to observe the properties of dyed sucralfate gel and assess the effectiveness of MCCE for direct real-time visualization of oral drug behavior in the stomach. They recruited 9 patients with a recent history of upper gastrointestinal symptoms and 10 healthy volunteers in the study. The results showed that compared to healthy controls, symptomatic patients showed shorter adhesion time and longer retention time of sucralfate gel. The distribution area of sucralfate gel in symptomatic patients was significantly larger in the cardia, fundus, and pylorus compared to other regions. The results confirmed that MCCE is a non-invasive tool for the real-time visualization of the intragastric behavior of orally administered drugs. Therefore, the performance and dynamic changes in delivering targeted drugs to specific regions of the gastrointestinal tract using MCCE should be further studied.

The MCCE design with biopsy function faces three challenges: precise positioning, navigating to the target location, and extracting multiple tissue samples.[50] To integrate biopsy functionality, Yim *et al.*[50] combined advanced navigation skills of centimeter-scale untethered MCCE with highly parallel, autonomous, submillimeter-scale tissue sampling μ-gripper to constitute a new wireless minimally invasive biopsy, called magnetically actuated soft capsule endoscope (MASCE). The MASCE system includes three main units: locomotion, delivery, and retrieval. It offers a multifunctional strategy for capsule biopsy of the gastrointestinal tract. However, it can only perform the biopsy of superficial tissues of the gastrointestinal tract, thus missing tumors in the subsurface of the gastrointestinal tract (e.g. submucosal tumors). Therefore, an accurate 3D positioning algorithm should be developed for improving the retrieval rate of the μ-gripper.

Son *et al.* proposed a magnetically actuated soft-capsule robot that uses fine-needle biopsy to collect samples from deep gastric tissues and perform *in vitro* experiments in the pig stomach.[51] The results showed an 85% biopsy rate for mock tumors located below the first layer of the stomach wall. Furthermore, tissues could be biopsied by positioning the system on the anterior, posterior, and lateral sides of the patient's stomach. Currently, this robot cannot generate magnetic forces sufficiently strong to conduct controlled probing or biopsies at arbitrary locations.

Capsule endoscopy can combine narrowband imaging, ultrasound, X-ray imaging, intelligent color enhancement, and optical coherence tomography to achieve optical biopsy.[13] Achieving biopsy at any location and in any orientation, including submucosal tumors, is the goal of future MCCE biopsy system development.

For Intestinal diseases. Chen *et al.*[25] used NaviCam to screen for small intestinal mucosal injury in asymptomatic patients on enteric-coated aspirin. They recruited 26 patients and 26 healthy people in the experimental and control groups, respectively. Compared to the control group, patients without obvious gastrointestinal symptoms had significantly higher rates of small intestinal mucosal injuries. Gastrointestinal injury is a common complication in patients on antiplatelet drugs after percutaneous coronary intervention. Li *et al.*[28] examined the incidence and severity of gastrointestinal mucosal injury in patients receiving different antiplatelet regimens using NaviCam. Among them, the cumulative incidence of gastrointestinal mucosal injury was 47% in patients receiving aspirin and P2Y12 inhibitor dual antiplatelet therapy (DAPT) for 12 months and 30% in those receiving aspirin or clopidogrel monotherapy and DAPT for 6 months, showing the superiority of the former in preventing gastrointestinal injury as detected by MCCE. This analysis showed that MCCE is a safe, real-time, and effective tool for assessing drug-induced small intestinal mucosal damage and could provide objective guidance for clinical treatment decisions.

MCCE can be also used to detect SB cleanliness. Ponte *et al.*[37] retrospectively included patients with incomplete exams performed between June 2009 and February 2016. Relative to regular capsule endoscopy, the new generation of SB cleanliness test uses a MiroCam® capsule endoscopy system with a battery life of 12 h instead of the 8 h previously reported for other capsule endoscopy systems, which allowed more tests to reach the cecum within the required time. Also, with the MiroCam® capsule endoscopy system, a diagnosis of a lesion in the distal small intestine can be derived.

In the case of small intestinal lesions, intestinal resection is a common treatment, but it usually leads to serious complications. Any tool or method that allows the selection of candidates and thus a more targeted and smooth 'delivery' of the Small Bowel Events Committee is a welcome approach. However, the selected capsule endoscopy tools should be cheap and easy to implement safely and quickly.[52] Considering all these issues, MCCE testing in combination with fecal validation testing can better identify the possibility of SB lesions.

Discussion

About meta-analysis of the review

Although this study provides a more comprehensive overview of MCCE by comparing it with the existing literature, the meta-analysis is not performed in the review. The deficiency is mainly caused by the following reasons:

First, it is difficult for us to look for the research data that are suitable for meta-analysis of the review. This is mainly because some key studies may not provide sufficient data or not publicly report sufficient statistical information, limiting our inclusion and further analysis of these studies. In addition, because some literature cannot pass our rigorous screening and evaluation requirements, they could not be included in the review.

Second, we encountered heterogeneity in study design and methodology during the review. There may be differences between studies in terms of experimental conditions, population characteristics, interventions, etc., which makes their inclusion in meta-analyses challenging. Although we used a rigorous literature screening and evaluation process, there may have been methodological flaws or biases in some studies that could have affected the accuracy and reliability of the results. This is another important reason why we did not use meta-analysis in our review.

Finally, I did not register this study with PROSPERO and will do so in future research.

The limitations of the MCCE

MCCE is in the primary stage of development, and clinical evidence for the detection of gastric lesions (particularly of gastric cancer) is limited. It does not have the advantages of conventional endoscopy in detecting gastric fluid, biopsy of lesions, or endoscopic treatment. MCCE with biopsy ability is in the basic research stage of preclinical application. Compared to conventional endoscopy, it takes a longer time to examine the gastrointestinal tract, has higher requirements for gastrointestinal preparation, and incurs a higher examination cost.

The further development of the MCCE

In the future research and development of MCCE, performance parameters (e.g. imaging resolution, examination time, etc.) should be improved. The accuracy and efficiency of automatic image interpretation algorithms with AI technology should also be increased. MCCE functions should be expanded to biopsy, treatment, local drug delivery, and drug behavior monitoring. A large number of samples should be used to validate its effectiveness and feasibility in the diagnosis and treatment of GID. In addition, reducing the cost of MCCE could popularize it for EGC screening in large populations. Multifunctional imaging is also a future direction for the improvement of MCCE.[13]

Conclusion

We comprehensively reviewed the development of MCCE, its ability to detect gastrointestinal lesions, factors related to imaging quality of MCCE, gastrointestinal endoscopy diagnosis with AI, as well as its other functions such as assessing drug behavior and drug injury to the mucosa and performing biopsy. Preliminary studies suggest that MCCE provides comparable clarity and visibility to conventional endoscopy in observing gastrointestinal mucosa in various regions while offering improved comfort and tolerance for patients. However, it is important to note that the findings regarding the performance of MCCE in detecting common gastrointestinal lesions are still based on limited evidence. Being a painless, noninvasive, safe, and hygienic examination technology, it has been gradually accepted by the public and especially it could have a good application prospect in EGC screening of large populations.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Author contributions

Xiaotong Wang: Formal analysis; Methodology; Writing – original draft.

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Yongxue Xu: Formal analysis; Investigation; Writing – original draft.

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Competing interests
The authors declare that there is no conflict of interest.

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