Efficacy and safety of magnetic guided capsule gastroscopy in gastric diseases

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Abstract

The current mainstay of screening and diagnosis for gastric diseases is conventional standard gastroscopy. However, it is invasive and uncomfortable procedure for the patients especially in case of non-sedative procedures and other adverse effects related to conscious sedation anesthesia. Recently, a magnetic guided capsule gastroscopy (MGCG) was introduced to overcome these challenges. It is a safe and pleasant procedure with no involvement of sedation and no risks of cross-infection between patients. In addition, this method is anticipated to be an alternative tool for screening and diagnosis of gastric diseases with similar gastric visualization as one achieved through standard gastroscopy. In this narrative review, we focused on the recent advances in MGCG including technical issues, ideal gastric preparation, indications and contraindications, available evidences regarding the use of magnetic guided capsule gastroscopy in clinical practice and highlighted further technical advancements which are needed to make MGCG as a potential diagnostic tool. After reviewing the literature, we concluded that the magnetic guided capsule gastroscopy is a safe tool and would be a promising alternative examination equipment for gastric diseases. (Acta gastroenterol. belg., **2019**, 82, **507-513**).

Keywords : Gastric diseases, magnetic guided capsule gastroscopy (MGCG), standard gastroscopy.

Introduction

Gastric diseases are very common globally with a wide variable range of distribution (1). Eastern Asia, Eastern Europe and some regions in Central and South America have a high incidence rate of gastric cancer compared to Western Europe and North America (2). Furthermore, gastric cancer is one of the fatal diseases presented in an advanced stage. In addition, it is the third leading cause of cancer death worldwide (3-6). In 2015, there were approximately 952,000 newly diagnosed cases and 754,000 deaths from gastric cancer worldwide (7). Almost 4% to 17% of the world population has a gastric or duodenal ulcer (8). The majority of gastric diseases are associated with Helicobacter pylori infection which occurs in asymptomatic individuals with approximately 50% prevalence rate worldwide (9). Due to the high magnitude of the gastric diseases, several strategies have been put in place to minimize the diseases. One of the strategies is the early detection by using various screening methods (10). The most commonly used screening method is gastroscopy which facilitates simultaneous visualization of gastric mucosa, performing a biopsy for further investigations and to offer resection of polyps and early cancer. Though it is regarded as a standard choice for screening, diagnosis and provision of therapy for many gastric diseases, it has some setbacks in terms of comfort and acceptability by patients (11-13). Also, it is considered as an invasive procedure because it needs intubation and involves high cost of sedative drugs (14). Another screening modality is a double-contrast barium radiography with photofluorography or digital radiography which can aid in the identification of malignant gastric ulcers, infiltrative lesions and other early gastric cancers (15,16). In addition, it is limited in effectiveness due to low sensitivity and false negative results (17,18). Other screening methods like serum pepsinogen, serum trefoil factor 3, microRNAs and multi-analytical blood tests have been suggested although further studies needed to verify their uses (19-21). Magnetic guided capsule gastroscopy is a non-invasive screening tool which allows complete visualization of the gastric wall (22). It offers two rotational and three translational kinds of motion and it can submerge and get closer to the mucosa for a clear view (23). The magnification of magnetic guided capsule gastroscopy is 1 :8 and through the guidance of the magnetic robot, the motion of capsule can be controlled as in figure 1 below (24). Based on the literature, it is regarded as an alternative screening and diagnostic tool with similar accuracy of the standard gastroscopy (25). This narrative review focuses on the current evidence regarding the efficacy and safety of magnetic guided capsule gastroscopy as a novel investigation tool to screen gastric diseases. We will comprehensively review previous studies and discuss the current status and future directions of MGCG.

Literature search for the present article

The literature search was performed in a line of narrative review but includes features of systematic review methodology. The electronic search includes three databases PubMed, EMBASE and Google Scholar, and use search terms “magnetic guided capsule gastroscopy OR magnetic assisted capsule gastroscopy OR magnetic steered capsule gastroscopy AND gastric diseases, OR

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stomach diseases, OR gastric disorders" the inclusion criteria was all type of articles published in PubMed which discussed about gastric diseases, magnetic guided capsule gastroscopy and are related only to humans. The exclusion criteria was articles for which full text was not available, not in English or were grey literature.

Description of the device

The complete magnetic navigation system consist of the following equipments : capsule incorporated with

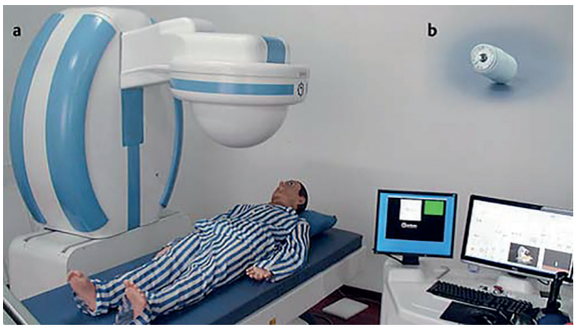

Figure 1. — The guidance equipment: A) guidance magnet robot and control panel; B) capsule reprinted with permission from Zou W-B et al.2015 .

Figure 2. — Olympus and Siemens navigation system (left) and the capsule (right). Reprinted with permission from Imdadur Rahman et al. 2015.

magnets and either controlled with a magnetic guidance system which uses a robotic arm or electromagnetic coil system or a handheld magnet which is hammer like as in figures 1, 2 and 3 (24,26). Currently in the clinical field, magnetic capsules guided by a robotic arms are preferable (27). Furthermore, it has been approved by the Chinese food and drug association and it can be used as follows : 1. as an alternative diagnostic tool for patients who refuse to undergo gastroscopy 2. Screening of gastric diseases as a part of physical examination 3. Screening for gastric cancer 4. To diagnose various causes of gastrointestinal inflammation 5. To perform follow-up for diseases like gastric varices, gastric ulcer, atrophic gastritis and polyps after surgical removal. On

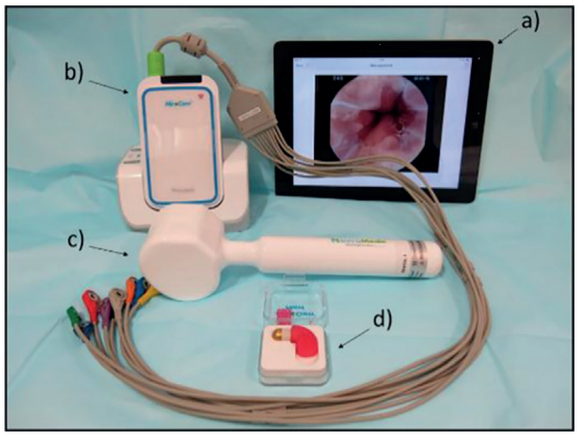

Figure 3. — (a) Real-time viewer, (b) sensors and receiver, (c) handheldmagnet, (d) MiroCam-Navi capsule. Reprinted with permission from Imdadur Rahman et al. 2015.

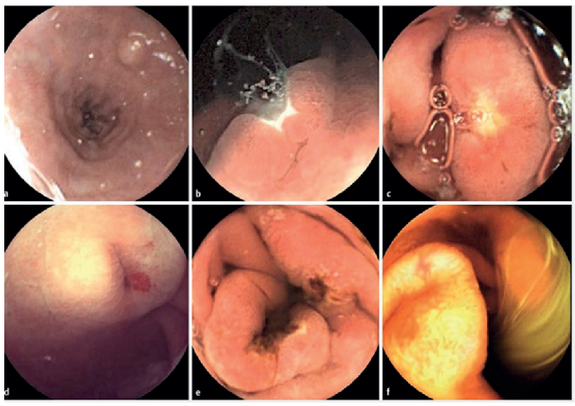

Figure 4. — Upper gastrointestinal tract abnormal findings viewed by magnetic guided capsule gastroscopy and missed by standard conventional gastroscopy a) Esophageal nodule b) mid part of body Gastric ulcer. c) Pre-pyloric gastric ulcer d) Gastric angioectasia e) ulcer at second part of duodenum f) angioectasia at second part of duodenum Adopted from Ching, Hey-Long et al (30).

the other hand, its contraindications includes patients with known or suspected gastrointestinal obstructions, strictures due to previous surgery, history of intestinal fistula and diverticulosis, patients with swallowing disorders, pregnant women and patients with implantable electro- medical devices like cardiac pacemakers or cochlear devices (28).

Technique of performing the magnetic guided capsule gastroscopy procedure

In order to perform a standard procedure, it requires a proper prior gastric preparation and changes in body position during the examination. Usually, three body positions are preferred that includes : left lateral, supine and right lateral positions for a clear vision of gastric mucosa. In addition, the patient is fasted for 8 to 12 hours

prior to the procedure and allow to drink water about 1000 ml thirty minutes to one hour before procedure for gastric distension (29). Furthermore, antifoaming agent (simethicone 40mg) is used to remove foams and bubbles 30 minutes to 1 hour before ingestion of a capsule. Afterwards, the patient drink a small amount of water together with capsule while staying in left lateral position in which the esophagus and gastroesophageal junction are observed clearly on this side. Once a capsule reaches the gastric cavity, several maneuvers are used. Firstly, the patient lies in a lateral position on the left side to observe the fundus, the body, the junction between the fundus and body, and the cardiac area in the far distant. Then, the patient turns into supine position to examine the anterior and posterior walls of the gastric body, cardiac region, greater and lesser curvatures, and angular notch. After, the patient moves to the right lateral side to visualize the antrum, pyloric region and the duodenal bulb(28). Currently there are no others consensus apart from Chinese expertise on the techniques of performing magnetic guided capsule gastroscopy.

MGCG complications

Magnetic guided capsule gastroscopy as compared to conventional capsule endoscopy has some complications which involves the swallowed capsule which can be accidentally enter in the airways during swallowing and causes aspiration which have been seen to occur in elderly patients and in those with swallowing disorders with a rate of 0.1% and incidence of about 1 in 600-700 patient procedures (30-32). Another frequently reported complication is retention of capsule which can occur in narrow parts of bowel lumen in about 1.5-2% as a result of crohn's disease, stricture and NSAIDs enteropathy that leads to relative intestinal obstruction. To overcome it patency ,capsule having capability to dissolve timely need to be introduced prior to swallow a magnetic capsule.(33, 34). Other rare minor complications which can arise due to gastric preparation prior to procedure examination includes nausea , vomiting, abdominal fullness or distension and feeling of foreign body sensation in gastrointestinal tract which could vanished within short time(35).

Magnetic guideed capsule gastroscopy versus esophagogastroduodenoscoy (EGD)

Table 1. — **MGCG**

ADVANTAGES	DISADVANTAGES
It is pleasant, non-invasive and well tolerated for patients with no pain or discomfort.	It cannot be done in patients with implantable electro-medical devices like cardiac pacemakers , cochlea hearing devices and also it cannot be done together with magnetic resonance imaging due to possibility of interference with magnetic forces which can lead to gastric mucosal injury(36).
It does not involve sedation effects.	It is a strenuous procedure for both patients and examiner with involvement of turning body positions to facilitate a clear view of some body parts.
No risk of contamination and cross infection between patients	It lacks air insufflation and sucking function hence involves complicated gastric preparation
it can be done in children of 8 years and above with comparable sensitivity for conventional capsule endoscopy (37).	It lacks capability to take tissue sample for histological and cellular investigations.
It can be simultaneously apply to visualize esophagus, stomach and small intestine with a high diagnostic yield of the diseases in these parts (38) (39).	It lacks therapeutic options like no ability to apply ablation, cauterization or resection procedures as EGD.
It can enhance small bowel capsule completion rate and reduce gastric transient time hence shorten the time to examine small intestine pathologies (40, 41).	Expertise are required in techniques of performing the procedure and in the results interpretation.
It can be perform without the presence of expertise personnel. Video can be recorded and downloaded and send to expertise for analysis and interpretation of results at any moment so it can save time in the community with low man power(42).	Hardware and software installation costs is high and even the capsule is not yet cost- effective to be afforded by many communities.

Table 2. — **Esophagogastroduodenoscopy (EGD)**

ADVANTAGES	DISAVANTAGES
It is a gold standard which accurately identify the location of lesions with functional capability of air insufflation and sucking for clear view.	It is invasive with involvement of pain and discomfort.
It offers tissue sampling collections so it save the purpose of the histological and cellular investigations	It involves sedation costs and adverse effects of sedative drugs.
It provides the options for therapeutic interventions like surgical resections and cauterization procedures.	there is possibility of contamination and cross infections among the patients if sterilization procedures are not conducted well, and also involve costs of sterilization procedures and manpower(43).
Procedure time is short not tiresome and it is cost-effective, easily affordable by many people in the community.	Sedative Patients need time to stay in hospital for recovery period which interferes with their daily activities.

Overview of gastric preparation protocol in MGCG

Considering the absence of air inflation and suction, clinical success of MGCG highly depends upon the degree of stomach cleansing. Accurate detection of lesions like polyps, ulcer or inflammation can only be achieved in a completely clean stomach without any kind of debris.

Currently, there is controversy on the standard optimal gastric preparation and mucosal visualization prior and during procedure respectively. There are several formulation agents and techniques which are employed when magnetic guided capsule gastroscopy is undertaken as diagnostic tool to examine gastric diseases. Currently adopted body positions in the technique to perform magnetic guided capsule gastroscopy are left lateral , supine and right lateral combination positions which were introduced by Rey et al (23) though they had low mucosal visualization rate in cardia and fundus position compared to a combination of five body position changes which were applied by Yuting Qian et al (44). Another technique was employed in a study done by Wang et al 2018 who compared the effectiveness of patient repetitive position changes and those who remained in the same position though the findings were in favour of repetitive position change group (45). But still there are challenges of both repetitive patient position changes and a combination of five body positions which are not in practical to be applied in elderly patients and it is tiresome and strenuous for the patients to undergo all body position changes and repetitive changes of position to the whole procedure maneuver. Furthermore when you consider different medication formulation agents to improve the gastric cleanliness to aid better mucosal visualization of all gastric landmarks and increase diagnostic yield of MGCG still there are contradicting school of thoughts and unmet needs of gastric preparation. The use of clear water and air producing powder had not proven to be effective to aid in gastric distension for better complete gastric visualization.(27, 46, 47). Yuting Qian et al study had better mucosal visualization at the cardia and fundus area which probably was contributed with the usage of simethicone , pronase granules and sodium Bicarbonate for gastric preparation which was contrary to Zhu, Qian, Tang et al study which focused in evaluation of quality of image by measuring attained gastric cleanliness and visualization score of three different preparation of water alone, water and simethicone , water ,simethicone and pronase. Among the preparation, the significance of quality of image was seen in water, simethicone side and water, simethicone and pronase side. But there were no significant added advantages of pronase as a mucolytic agent which rises some questions if it is important to consider pronase in combination with simethicone for gastric preparation or we can just rely on water and simethicone only though the study sample size was small to justify the evidence of the findings. Another gap of knowledge is which dose for sodium bicarbonate is favorable to keep the gastric PH in alkaline condition for pronase as mucolytic agent to function in effective ways.(48). Another unresolved issue is amount of water patients should ingest to facilitate the completion of procedure and the optimal agreed time interval, as many scholars advocated the range from 500ml to 1000ml in two or three portions with a time interval of one hour, two or three hours before procedure.

Clinical trials and studies on the efficacy and safety of MGCG in gastric diseases

The accuracy of magnetic guided capsule gastroscopy has been demonstrated in a comparative single center blinded non-randomized human clinical trial done by Rey et al. who involved 61 patients who had an indication for standard gastroscopy (49). A total of 108 pathological findings were diagnosed, among them, 63 (58.3%) were matched with both standard gastroscopy and magnetic guided capsule gastroscopy (49). Furthermore, based on the two diagnostic modalities, the magnetic guided capsule gastroscopy detected 31 lesions that were not picked up by the standard gastroscopy (49). On the other hand, the standard gastroscopy picked up 14 lesions that did not appear on the magnetic guided capsule gastroscopy (49). The possible explanation is that the magnetic guided capsule gastroscopy examination took longer time with a mean of 17.4 minutes compared to standard gastroscopy with a mean of 5.3 minutes (49). In their study, the standard gastroscopy was performed prior to the magnetic guided capsule gastroscopy which leads to mucosal injuries from the intubation and biopsy (49). Additionally, to further explore the accuracy of MGCG in gastric diseases, another two comparative clinical trials were conducted in France and China(24, 50).In these trials, all patients (100%) were subjected to MGCG before the standard gastroscopy (24,50). In the first clinical trial, the researchers categorized the pathological findings as major lesions (which involve biopsy) and minor lesion (where no tissue samples were needed) (50). Moreover, 23 major lesions were found including gastric ulcer =9, focal angiodysplastic=5, submucosa tumors=4, single hyperplasic polyps=3, and 2=adenocarcinoma (50). As for minor lesions, it includes diffuse inflammation n=165, multiple fundic polyps n=55 atrophic gastritis n=16. Additionally, the diagnostic accuracy was determined based on sensitivity and specificity of major and minor lesions which was 61.9% to 94.1% for major and 89.2% to 70% for minor lesions(50). As for the second clinical trial, 68 pathological lesions were recognized, among them 53 were matched for both modalities (24). The standard gastroscopy revealed extra 7 lesions (3 erosions, 2 ulcers, 1 atrophy and 1 mucosal protuberance) that were not detected by magnetic assisted capsule gastroscopy (24). On the other hand, magnetic assisted capsule gastroscopy identified 8 lesions (6 erosions, 1 polyp

and 1 mucosal protuberance)that were not observed by the standard gastroscopy (24). Ultimately, there was no superior diagnostic modality in both trials (24,50). To further determine the accuracy of diagnosis of magnetic controlled capsule gastroscopy versus conventional gastroscopy another prospective blinded multicenter study was conducted in China by Liao et al(35). The study involved 350 patients and MGCE detected gastric focal lesions like a malignant tumor, benign tumor and gastric ulcer >5mm with an accuracy of 93.4%, sensitivity of 90.4% and specificity of 94.7% (35). The results were comparable to conventional gastroscopy and the crucial role of MGCG as a filter test to categorize patients prior to standard gastroscopy was revealed (35). In 2018,Zhao et al. published a retrospective observational cohort multicenter study which involved 3182 asymptomatic individuals who were subjected to MGCG (51). The aim of the study was to determine the detection rate of gastric cancer and focal lesions (51), gastric cancer was found in **7** patients (0.22%) and all of them were above 50 years (51). The subsequent standard gastroscopy and biopsy confirmed the diagnosis as adenocarcinoma (51). Moreover, focal lesions were found in 567 patients with 36 patients (17.8%) having multiple lesions, 331 patients (10.4%) having benign polyps, 156 patients (4.9%) having gastric ulcer and 115 patients (3.6%) with submucosal tumors (51). Overall, the diagnostic accuracy of MGCG was consistent with other previous studies (24,35,49-51). In addition, more evidences on the effectiveness of magnetic guided capsule gastroscopy to identify gastric lesions were revealed in another retrospective study which involved inpatients and outpatients a total of 580 patients who underwent MGCG (52). The findings of MGCG were categorized into three groups including the absence of pathological lesions, minor lesions and major lesions (52). In addition, polyps, ulcers, stricture, gastric mass and angiodysplastic lesions were regarded as major lesions (52). Higher yield of polyps , mass, or stricture (20.2% cf. 13.3%, *P*= 0.03) and higher yield of ulceration (20.2% cf. 11.2%, *P*= 0.003) were demonstrated in comparative results of inpatients and outpatients (52) .

Limitations and future directions

Currently, magnetic guided capsule gastroscopy is facing challenges such as shortage of air insufflation, suction, acquisition of tissue samples, provision of drugs on the site of pathology and ability to offer therapeutic procedure options. Additionally, the attention of many researchers focused on overcoming the aforementioned challenges. Moreover, the acquisition of a tissue biopsy by the capsule which is microscopically capable to grasp, carry, release the tissue and retrieve the capsule instrument has been established and tested in ex vivo in animal models with possibility to be perform in vivo in animals in the future before embarking it to human beings (53).

The possibility of magnetic guided capsule gastroscopy to be controlled and held in one place is useful through delivering the drugs to specific sites in the human gastrointestinal mucosa. Moreover, it has been supported by the development of a therapeutic capsule which is controlled by an external permanent magnetic source (54,55).

Furthermore, more advancements has been achieved in dealing with the challenges of air insufflation in the gastrointestinal lumen. In the near future, the physicians are expecting to see magnetic guided capsule gastroscopy incorporated with air insufflations capability to produce a large amount of carbon dioxide (co_2) from a small amount of liquid (weak acid and/or base) to inflate the gastrointestinal lumen and aids in visualization (56,57).

Magnetic guided capsule gastroscopy has potential to be more effective as compared to the passive capsule endoscopy. Additionally, it can overcome the challenges of rapid motion and can delay the emptying of the capsule with its active control mechanism. Also, the capsule can be pause to create enough time to study gastrointestinal mucosa. Besides, it is very helpful for the elderly people who are more prone to get esophageal diseases like gastroesophageal reflux diseases(GERD),Barrett esophagus and esophageal varices (58,59). Another concern is magnetic guided capsule gastroscopy is safe to be performed in patients with metallic parts or implants as the capsule need small magnetic force to operate, 3-10mT which is 15 times smaller than magnetic resonance image (MRI). On the other hand, the guidance system does not produce heat or need a cooling system as in MRI, hence causes no side effects for patients(50). Unfortunately, the current evidences are not strong enough and more studies are needed to overcome the challenges.

At present, the magnetic guided capsule gastroscopy is in the initial phase of implementation in many clinical settings around the world. Its cost is high especially hardware parts and software installation which costs €20,070 and a disposable capsule costs €401 (60). However as the time goes on, the physicians around the world would expect it to be cost-effective and more acceptable by the patients with no involvement of sedation (50). Unlike esophagogastroduodenoscopy (conventional standard gastroscopy) procedure which involves sedation and causes indirect costs by making the patients unable to perform daily activities during the daytime of gastric examination, EGDs costs €1282 with sedation and €857 without sedation (61).

Conclusion

Magnetic guided capsule gastroscopy (MGCG) is a new technology in the gastrointestinal field. In addition, it shows promising results in the endoscopic practice as it is a non-invasive procedure which is pleasant for patients and has no involvement of sedation. Furthermore, it has potential to be use as an alternative tool for early screening and diagnosis of gastrointestinal tract diseases. However,

there are certain issues which needs to be clarify before it can be prove as a worthy and competent procedure. Large randomized clinical trials are needed which can discern an optimal gastric preparation for magnetic guided capsule gastroscopy procedure and target specific gastric diseases like gastric cancer, gastric ulcer or gastritis to determine its ability and also to clarify issues of safety in patients with metallic body parts or implanted devices.

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Conflict of interest

None.

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