Animal Experimental Study on Magnetic Anchor Technique-Assisted Endoscopic Submucosal Dissection of Early Gastric Cancer

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Research Article

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Abstract

Background

Gastric cancer (GC) has high morbidity and mortality. Moreover, because GC has no typical symptoms in the early stages, most cases are already in the advanced stages by the time the symptoms appear, thus resulting in poor prognosis and a low survival rate. Endoscopic submucosal dissection (ESD) can realize the early detection and diagnosis of GC and become the main surgical method for early GC. However, ESD has a steep learning curve and high technical skill requirements for endoscopists, which is not conducive to its widespread implementation and advancement. This study aimed to evaluate the safety and efficacy of magnetic anchor technique (MAT)-assisted ESD in early GC.

Method

This was an ex vivo animal experiment. The experimental model was the isolated stomachs of pigs. The magnetic anchor device for auxiliary ESD comprised three parts, an anchor magnet (AM), a target magnet (TM), and a soft tissue clip. Under gastroscopic guidance, the soft tissue clip and the TM were delivered to the pre-marked mucosal lesion through the gastroscopic operating hole. The soft tissue clip and the TM were connected by a thin wire through the TM tail structure. The soft tissue clip was released by manipulating the operating handle of the soft tissue clip in a way that the soft tissue clip and the TM were fixed to the lesion mucosa. In vitro, ESD is aided by maneuvering the AM such that the mucosal dissection surface is exposed.

Result

During the operation, there was no detachment of the soft tissue clip and TM and no mucosal tearing. The magnetic force between the AM and TM provided good mucosal exposure and sufficient tissue tension for ESD. The mucosal lesion was completely peeled off, and the operation was successful.

Conclusion

MAT-ESD is safe and effective for early gastric cancer. It provides a preliminary basis for subsequent internal animal experiments and clinical research.

Background

Cancer continues to be an immense threat to human health and exerts a huge medical and economic burden. In 2020, there were more than 1 million new cases of gastric cancer (GC) and an estimated 769,000 deaths (equivalent to 1 in 13 deaths globally). GC has the fifth-highest incidence and the fourth-highest mortality of all cancers worldwide [1]. Due to its large population, China accounts for
approximately 44% of GC cases worldwide, and in 2020, GC in China had an adjusted incidence rate of 20.6/100,000 individuals [2]. GC is usually at an advanced stage by the time the symptoms appear, which leads to a poor prognosis. Although the 5-year survival rate for advanced GC is 10%, the 5-year survival rate for early GC can be as high as 85% [3]. Therefore, it is possible to carry out population-based screening in high-risk areas or high-risk groups to achieve early detection, diagnosis, and treatment of GC, thus reducing the burden of GC on public health. The use of endoscopy screening in high-risk groups can reportedly significantly reduce GC mortality [4, 5]. At present, the 5-year survival rates of GC in Japan and South Korea are relatively high at 60.3% and 68.9%, respectively [6]. These rates are attributed to the effectiveness of large-scale endoscopic screening programs, which help identify a higher proportion of early GC cases at the time of screening [7, 8].

The primary treatment option for early GC is endoscopic therapy, which includes endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) [9, 10]. ESD is developed on the basis of EMR and is used for dissecting large tumor lesions that are not suitable for EMR [11]. Compared with EMR, ESD has higher en bloc resection rates (90.2% vs. 51.7%), higher histologic complete resection rates (82.1% vs. 42.2%), and lower recurrence rates (0.65% vs. 6.05%) [12]. However, ESD is not like traditional surgery, and as the surgeon's hand cannot enter the alimentary canal lumen, it is difficult to obtain sufficient tension and good field. These challenges result in a long operation time, high risk of adverse events, and high incidence of postoperative complications (bleeding and perforation) [13]. Therefore, to circumvent these challenges and avoid these complications, many assistive technologies have been developed [13], such as the clip-with-line method [14], pulley method [15, 16], sheath traction method [17, 18], external forceps method [19, 20], double scope method [21], the S–O clip [22, 23], ring thread countertraction [24], multiloop technique [25], double clip and rubber band traction [26], clip band technique [27], pocket creation method with a traction device [28], and clip-flap method [29]. However, these auxiliary techniques have some disadvantages, such as inflexibility in changing the magnitude of the traction force, a single direction of the traction force, and inability to resect any lesion regardless of its location.

Magnetic anchor technique (MAT)-assisted ESD is a new type of assistive technology with some potential advantages, such as control over traction direction and traction size. It was first proposed by the Japanese scholar Kobayashi [30] in 2004. The magnetic anchor system includes internal and external magnetic components. The outer magnetic assembly is usually a permanent magnet, and the inner magnetic assembly includes an inner magnet and a tissue clip [31]. MAT-ESD has been successfully applied to various thoracoscopy and laparoscopy procedures, such as laparoscopic cholecystectomy [32] and thoracoscopic lobectomy [33]. The application of this technique reduces surgical trauma and interference between surgical instruments, thus improving the exposure of the surgical field and the operability of the surgery [31]. Therefore, in this study, we explored the safety and feasibility of MAT-ESD in early gastric cancer in an in vitro porcine model using the self-designed magnetic anchor device.

**Materials And Methods**
Magnetic anchor device

The self-designed magnetic anchor device made by Shaanxi Jinshan Electric Co., Ltd. comprises three parts (Fig. 1): the anchor magnet (AM), the target magnet (TM), and the soft tissue clip. The AM is a cylinder made of the Nd–Fe–B permanent magnet material, and the surface is protected by nickel plating. To avoid interference from other ferromagnetic objects during use, the AM cylinder is covered with a 5-mm U-shaped resin shell. The AM is located outside the body and is used to pull the TM. The AM is 140-mm high and has a base diameter of 50 mm and a surface field strength of 6000 GS. The TM is also made of the Nd–Fe–B permanent magnet material. The TM is divided into a cylindrical magnetic core and a permalloy shell. The surface is coated with nickel or titanium nitride. The TM is located inside the body. To adapt to the size of the digestive tract, the magnetic core is a cylinder with a height of 5.5 mm and a bottom diameter of 4 mm, and the surface field strength is 3000 GS. In addition, the permalloy tail has a circular hole structure with a diameter of 1 mm for connection with soft tissue clips. The soft tissue clip is processed by the Micro-Tech (Nanjing) Co., Ltd. It can be connected to the tail end structure of the TM through a thin wire, and the TM can be fixed to the lesion mucosa.

Animals

This was an *ex vivo* experiment. The pigs were obtained from the Experimental Animal Center of Xi’an Jiaotong University. The isolated pigs’ stomachs were obtained from euthanized pigs by an intravenous overdose of sodium pentobarbital (30 mg/kg) after the end of other experimental projects by our team. We used stomachs isolated from six Bama miniature pigs (three males and three females) for our experiments. The sex of the animal was not a factor in data analyses. The IUCN Policy Statement on Research Involving Species at Risk of Extinction and the Convention on the Trade in Endangered Species of Wild Fauna and Flora were followed. The pigs used in this study complied with the guidelines of the American Veterinary Medical Association (AVMA) Guidelines for the Euthanasia of Animals (2020). The experimental protocol was approved by the laboratory animal care committee of Xi’an Jiaotong University (approval NO. XJTULAC2019-1006) and was in accordance with the ethical standards for experimental animals of Xi’an Jiaotong University. The fundamental principles and the ethical guidelines of the Basel Declaration and the International Council for Laboratory Animal Science (ICLAS) for conducting research in laboratory animals were followed. All animal experiments were carried out in accordance with the revised Animals (Scientific Procedures) Act 1986 in the UK and Directive 2010/63/EU in Europe. All animal experiments complied with the ARRIVE guidelines and were carried out in accordance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals (eighth edition, 2011).

Surgical procedure

On the basis of the end of other animal experiments, the isolated pig stomachs were obtained, and about 5 cm of the esophagus and duodenal stump was retained. First, the duodenal stump was clamped with intestinal forceps, and then, a gastroscope was inserted from the esophageal stump to inflate and observe the airtightness of the stomach and the integrity of the mucosa (Fig. 2A). Second, the mucosal
lesion to be resected was marked by electrocautery under gastroscopic guidance (Fig. 2B). Third, the TM was fixed to the mucosal lesion by a soft tissue clip. The soft tissue clip was inserted through the operation hole of the gastroscope, and the TM was connected to the soft tissue clip with a thin wire; however, the TM did not affect the opening and closing of the soft tissue clip (Fig. 2C). Finally, the magnetic force between TM and AM was used to expose the mucosal dissection surface and maintain tissue tension. The AM was gradually brought close to the stomach in vitro, and the state of the TM was observed using the endoscope (Fig. 2D). The TM was seen to be pulled toward the AM, and at the same time, the soft tissue clip was driven to lift the lesion mucosa. The position of the AM was adjusted according to the operation requirements, and the pulling direction and strength of the mucosal lesion were flexibly changed until the lesion was completely removed (Fig. 2E, 2F).

**Results**

By clamping the duodenal stump, the isolated stomach was made airtight, and the mucosa was intact. After the mucosal lesion was successfully marked, the gastroscope, the TM, and the soft tissue clip were smoothly entered into the stomach through the digestive tract and advanced until the lesion was reached. During the entire operation, the soft tissue clip was tightly connected with the TM to avoid falling off or separation, and the TM did not affect the opening, closing, and release of the soft tissue clip. Furthermore, surgical instruments, except the AM and TM, were not disturbed by the magnetic force. By changing the position of the AM, the pulling direction and pulling force of the soft tissue clip could be easily changed, the mucosal dissection surface was well exposed, and sufficient tension was maintained. In addition, the soft tissue clip did not fall off and the mucosa was not torn. Finally, the marked mucosal lesion was completely stripped, and the operation was successfully completed (Fig. 2).

**Discussion**

Our results emphasize the safety and efficacy MAT-ESD in early gastric cancer. Six operations were successfully completed, and in all of these operations, the mucosal lesion was completely peeled off without tearing of the mucosa or detachment of the TM and soft tissue clip.

The MAT belongs to the category of magnetic surgery. It is currently an auxiliary technique for ESD with great application prospects. The MAT primarily uses the magnetic force between the magnets, and this helps overcome the disadvantage of ESD being difficult to operate and also gives the endoscope operator a “third hand.” The magnetic materials used in the magnetic anchor system are primarily electromagnets and permanent magnets [34]. For electromagnets, the intensity of the magnetic field can be controlled by changing the amount of electricity. However, they are large and bulky, making it challenging to use them in the narrow digestive tract. Conversely, high-performance permanent magnets are based on compounds with excellent intrinsic magnetic properties and optimized microstructure and alloy composition. At present, the most powerful permanent magnet materials are RE–TM intermetallic alloys, which derive their exceptional magnetic properties from the favorable combination of rare earth metals (RE = Nd, Pr, and Sm) with transition metals (TM = Fe and Co); specifically, magnets based on (Nd, Pr)$_2$Fe$_{14}$B and
Sm$_2$(Co, Cu, Fe, Zr)$_{17}$ are particularly good permanent magnets [35]. In addition, considering the low corrosion resistance of neodymium magnets, which is of particular concern in the acidic environment of the stomach, and the possibility of interference of the magnetic field with other surgical instruments, the shielding material used must be inert to the human body and unobstructed to the magnetic field, such as titanium alloys, ring oxygen resin, or a copper-based alloy (with additional coating) [34].

The TM used in previous studies is a simple magnetic ring [36–38], whereas our TM uses permanent magnets (Nd–Fe–B) and a permalloy shell to shield the impact of magnetic fields on surgical instruments and people, thus enhancing the attraction between the AM and TM. Finally, the size of the TM was optimized considering the size of the digestive tract and the physiological environment, and the tail suspension structure was designed for connection with the soft tissue clip considering both the characteristics of the digestive tract and magnetic requirements.

The main disadvantage of this experiment is that it was an external experiment, and the findings may differ in an internal animal experiment or a clinical study. However, we were unable to assess the risk of postoperative complications, such as bleeding, perforation, and strictures. Second, because the abdominal thickness in human beings differs from that in pigs, our findings cannot help predict the effect of abdominal wall thickness when this technique is applied to humans. Third, because the mucosal lesion is marked by the experimenter and is subjective, it was not possible to evaluate the influence of surgery on the size and location of the lesion.

However, MAT has shown great clinical potential when used as an auxiliary technique for ESD. The results of this study show that MAT-ESD is safe and effective. This study lays a solid foundation for the next animal experiment and clinical study and provides a preliminary foundation for the accuracy and optimization of the magnetic anchor device.

**Conclusion**

The safety and efficacy of MAT-ESD have been demonstrated in early gastric cancer, albeit only in external animal experiments. However, MAT shows advantages over other assistive technologies, such as flexibility to change the magnitude and direction of traction. This method shows great auxiliary potential in ESD and has good prospects for clinical application.

**List Of Abbreviations**

GC  
gastric cancer  
ESD  
endoscopic submucosal dissection  
MAT  
magnetic anchor technique
Declarations

Ethics approval and consent to participate

The IUCN Policy Statement on Research Involving Species at Risk of Extinction and the Convention on the Trade in Endangered Species of Wild Fauna and Flora were followed. The pigs used in this study were complied with the guidelines of the American Veterinary Medical Association (AVMA) Guidelines for the Euthanasia of Animals (2020). The experimental protocol was approved by the laboratory animal care committee of Xi’an Jiaotong University (approval NO. XJTULAC2019-1006) and was in accordance with the ethical standards for experimental animals of Xi’an Jiaotong University. The fundamental principles and the ethical guidelines of the Basel Declaration and the International Council for Laboratory Animal Science (ICLAS) for conducting research in laboratory animals were followed. All animal experiments were carried out in accordance with the revised Animals (Scientific Procedures) Act 1986 in the UK and Directive 2010/63/EU in Europe. All animal experiments complied with the ARRIVE guidelines and were carried out in accordance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals (eighth edition, 2011).

Consent for publication (Not applicable)

Availability of data and materials

The datasets underlying the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors’ contributions

Y.L. and X.Y. conceived and designed the study; M.P. and M.Z. performed the research and acquired the data; L.Z. wrote the manuscript; M.P. and M.Z. revised the manuscript; Y.L. and X.Y. examined the final manuscript; All authors read and approved the final manuscript.

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References


**Figures**

**Figure 1**

Magnetic anchor device.

**Figure 2**

Magnetic anchor technique-assisted ESD operation process. **A.** The isolated stomach was examined using a gastroscope. **B.** The mucosal lesion to be resected was marked by electrocautery under gastroscopic guidance. **C.** The TM and the soft tissue clip were connected and placed in the gastric...
lumen and the soft tissue clips clamped the mucosa. D. AM was placed outside the stomach. Under the attraction of the AM, the TM hangs in the stomach cavity and pulls the mucosa. E and F. The mucosal lesion has been stripped.