

Basic Study

Magnetic anchor technique assisted endoscopic submucosal dissection for early esophageal cancer

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Grade E (Poor): 0**P-Reviewer:** Cho JY, South Korea; Osawa S, Japan**Received:** August 19, 2023**Peer-review started:** August 19, 2023**First decision:** August 31, 2023**Revised:** September 12, 2023**Accepted:** September 25, 2023**Article in press:** September 25, 2023**Published online:** October 16, 2023**Min Pan, Miao-Miao Zhang, Shu-Qin Xu, Yi Lyu, Xiao-Peng Yan**, Department of Hepatobiliary Surgery, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an 710061, Shaanxi Province, China**Min Pan**, Department of Thoracic Surgery, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an 710061, Shaanxi Province, China**Miao-Miao Zhang, Shu-Qin Xu, Yi Lyu, Xiao-Peng Yan**, National Local Joint Engineering Research Center for Precision Surgery & Regenerative Medicine, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an 710061, Shaanxi Province, China**Corresponding author:** Xiao-Peng Yan, MD, PhD, Associate Research Scientist, Department of Hepatobiliary Surgery, The First Affiliated Hospital of Xi'an Jiaotong University, No. 277 West Yanta Road, Xi'an 710061, Shaanxi Province, China. yanxiaopeng9966@163.com

Abstract

BACKGROUND

Esophageal cancer has high incidence globally and is often diagnosed at an advanced stage. With the widespread application of endoscopic technologies, the need for early detection and diagnosis of esophageal cancer has gradually been realized. Endoscopic submucosal dissection (ESD) has become the standard of care for managing early tumors of the esophagus, stomach, and colon. However, due to the steep learning curve, difficult operation, and technically demanding nature of the procedure, ESD has currently been committed to the development of various assistive technologies.

AIM

To explore the feasibility and applicability of magnetic anchor technique (MAT)-assisted ESD for early esophageal cancer.

METHODS

Isolated pig esophagi were used as the experimental model, and the magnetic anchor device was designed by us. The esophagi used were divided into two groups, namely the operational and control groups, and 10 endoscopists completed the procedure. The two groups were evaluated for the following aspects: The total operative time, perforation rate, rate of whole mucosal resection, diameter of the peering mucosa, and scores of endoscopists' feelings with the procedure, including the convenience, mucosal surface exposure degree, and tissue tension.

In addition, in the operational group, the soft tissue clip and the target magnet (TM) were connected by a thin wire through a small hole at the tail end of the TM. Under gastroscopic guidance, the soft tissue clip was clamped to the edge of the lesioned mucosa, which was marked in advance. By changing the position of the anchor magnet (AM) outside the esophagus, the pulling force and pulling direction of the TM could be changed, thus exposing the mucosal peeling surface and assisting the ESD.

RESULTS

Herein, each of the two groups comprised 10 isolated esophageal putative mucosal lesions. The diameter of the peering mucosa did not significantly differ between the two groups (2.13 ± 0.06 vs 2.15 ± 0.06 , $P = 0.882$). The total operative time was shorter in the operational group than in the control group (17.04 ± 0.22 min vs 21.94 ± 0.23 min, $P < 0.001$). During the entire experiment, the TM remained firmly connected with the soft tissue clip and did not affect the opening, closing, and release of the soft tissue clip. The interaction between the TM and AM could provide sufficient tissue tension and completely expose the mucosa, which greatly assists the surgeon with the operation. There was no avulsion of the mucosa, and mucosal lesions were intact when peeled. Therefore, the scores of endoscopists' feelings were higher in the operational group than in the control group in terms of the convenience (9.22 ± 0.19 vs 8.34 ± 0.15 , $P = 0.002$), mucosal surface exposure degree (9.11 ± 0.15 vs 8.25 ± 0.12 , $P < 0.001$), and tissue tension (9.35 ± 0.13 vs 8.02 ± 0.17 , $P < 0.001$). The two groups did not significantly differ in the perforation rate and rate of whole mucosal resection.

CONCLUSION

We found MAT-assisted ESD safe and feasible for early esophageal cancer. It could greatly improve the endoscopic operation experience and showed good clinical application prospects.

Key Words: Magnetic surgery; Magnetic anchor technique; Magnetic anchor device; Endoscopic submucosal dissection; Early esophageal cancer

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Core Tip: Esophageal cancer has high incidence globally and is often diagnosed at an advanced stage. Owing to the increased adaptation of endoscopic submucosal dissection (ESD), early diagnosis and treatment of esophageal cancer have improved. However, there are some limitations of ESD, such as a steep learning curve, longer surgical time, higher risk, and more complications. Magnetic anchor technique is a brand new ESD assistance technique with great potential in shortening the surgical time, improving endoscopists' satisfaction, and providing sufficient tissue tension and perfect mucosal exposure, indicating that it has good prospects for clinical application.

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INTRODUCTION

According to GLOBOCAN 2020 data, esophageal cancer is among the most common cancers worldwide; it ranks seventh in terms of incidence and is the sixth leading cause of cancer deaths[1]. In most cases, early esophageal cancer and precancerous lesions can be cured by minimally invasive endoscopic treatment, and the 5-year survival rate can reach 95%[2]. However, patients with advanced esophageal cancer have a low quality of life and poor prognosis, and their overall 5-year survival rate is < 20%[3]. Because esophageal cancer is usually not diagnosed until an advanced stage, there are few options available to extend life expectancy beyond several months[4]. Therefore, it is very important to improve the screening methods for early esophageal cancer.

Endoscopic resection includes endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD). ESD was developed on the basis of EMR in Japan and has become the standard of care for managing early tumors of the esophagus, stomach, and colon[5]. Compared to EMR, ESD can offer better outcomes, lower morbidity, lower cost, higher curative resection rates, and lower recurrence rates[5,6]. ESD is performed using an endoscope, which makes the procedure technically challenging[7-11]. Consequently, ESD has a steep learning curve, longer surgical time, higher risk, and more complications (*e.g.*, bleeding, pain, perforation, and stricture) than EMR[12]. In addition, for effective and safe dissection, adequate tissue tension and a clear anatomical plane are important[11-14]. To overcome these abovementioned challenges associated with the use of ESD, scholars have proposed several auxiliary methods of pulling mucosa, such as percutaneous traction-assisted method[15], sinker system traction-assisted method[16], mucosal forceps channel-assisted method[17], S-O clip traction-assisted method[18], "medical ring" traction-assisted method[19], a Master and Slave

Translumenal Endoscopic Robot[20], a novel flexible endoscopic surgical platform[21], and dual-scope endoscopic dissection method[22]. Although these methods play a certain role in ESD operation, their flexibility in controlling mucosal traction direction and traction force is poor, and some endoscopic platforms are still difficult to be clinically used on large scale.

Magnetic anchor guided-ESD (MAG-ESD) is a new type of assistive technology that functions using a special traction force, which confers its potential advantages over other assistive technologies[5]. In 2004, Kobayashi *et al*[11] applied the principle of magnetic anchor technique (MAT) to ESD and reported that this technique significantly improved endoscopic operation. MAG-ESD provides dynamic tissue contraction independent of the endoscope, thus mimicking the surgeon's two hands[5]. A magnetic anchor comprises three parts: A hand-made magnetic weight made up of magnetic stainless steel, micro forceps, and a connecting thread that connects a hand-made magnetic weight made up of magnetic stainless steel with micro forceps[19]. Two types of magnets can be used: Electromagnets and permanent magnets[23]. Presently, MAG-ESD is known to have achieved significant results in gastric cancer[24] and colorectal cancer[25], proving its safety and feasibility for promoting ESD of early cancer. In this article, we will elaborate on the use of MAT-assisted ESD in early esophageal cancer.

MATERIALS AND METHODS

Animals

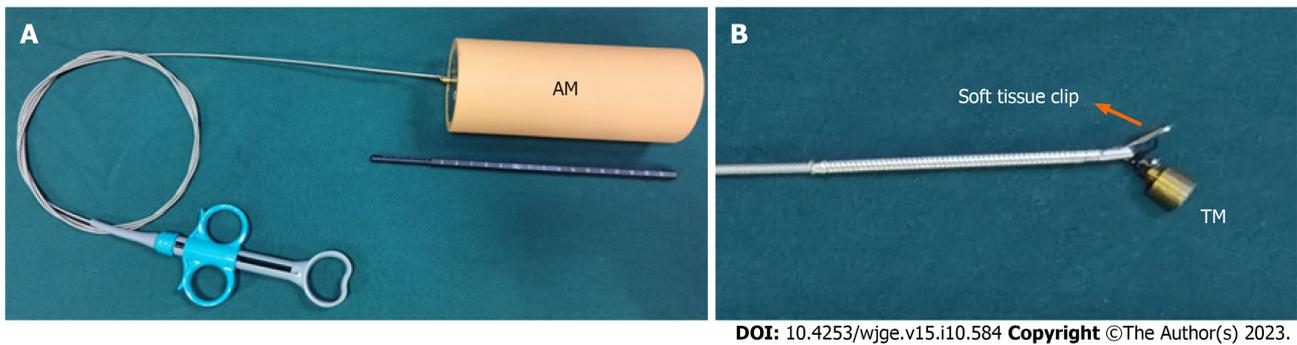
This was an *in vitro* animal experiment performed on isolated esophagi of 20 pigs divided into two groups, namely the operational group and control group. The pigs were obtained from the Experimental Animal Center of Xi'an Jiaotong University. We used the pigs that were euthanized by a professional veterinarian after other experimental projects of our team. Notably, since these projects were not related to the digestive system, they had no effect on the physiological function and anatomical structure of the esophagus, and the pigs remained suitable for this present experiment. All pigs were Bama miniature pigs aged 1-2 years and weighed 20-25 kg. The male:female ratio of the pigs was 1:1. Besides, the experiment was approved by the animal experiment ethics committee of Xi'an Jiaotong University (No. XJTULAC2019-1006). 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).

Magnetic anchor device

The magnetic anchor device used in this experiment was designed by us and fabricated by Shaanxi Jinshan Electric Co., Ltd. It comprises three parts: The target magnet (TM), the anchor magnet (AM), and the soft tissue clip. TM is a "passive force" part located in the esophagus, and its shape and size are limited by the digestive tract's lumen. The surface field at both ends of the magnet is 3000 GS. The permalloy shell is U-shaped with a 1-mm wall thickness. The diameter of the cylindrical magnetic core is 4 mm, and the height is 5.5 mm. In addition, the tail end also has a tail hanging structure. A tail hanging structure with a 1-mm hole can be connected to the soft tissue clip using a silk wire. The AM is the "active force" part and is located outside the isolated esophagus; its shape and size are less limited since it is not placed inside the lumen. The AM is cylindrical with a diameter of 50 mm and a height of 140 mm, and the surface magnetic field intensity at both ends of the magnet is 6500 GS. In addition, to avoid mutual attraction between the AM and ferromagnetic objects during use, the AM is covered with a layer of a U-shaped resin shell with a thickness of 5 mm. The TM and AM are made of N48 sintered NdFeB permanent magnet material; they are nickel-plated on the surface. The soft tissue clip, also known as the harmony clip (Nanwei Medical Technology Co., LTD.), can be closed to fix the TM on the pathological mucosa (Figure 1). The variation of magnetic force with distance between AM and TM was measured using an electronic universal testing machine (UTM6202, Shenzhen Suns Technology Stock, Figure 2).

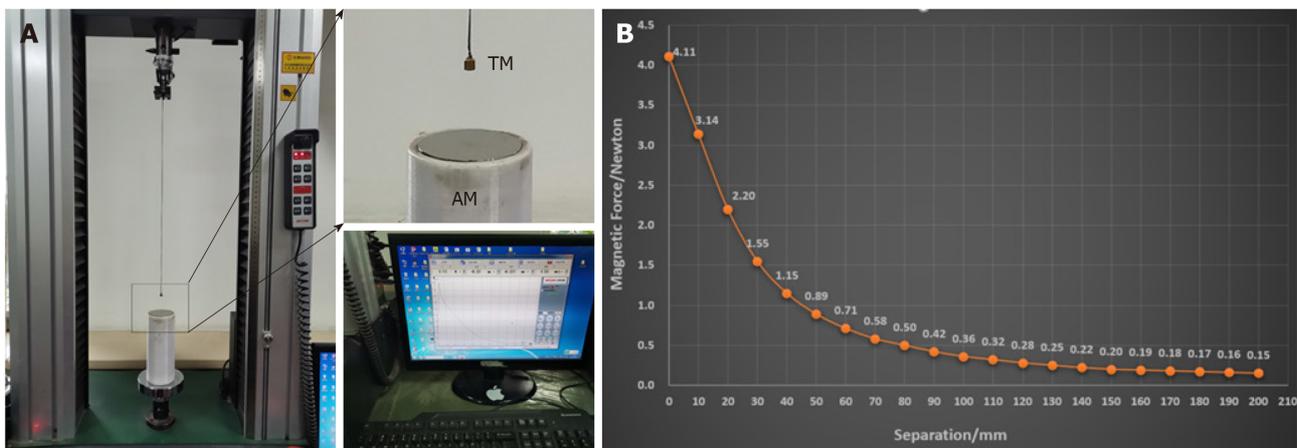
Operational process

The isolated pig esophagus was placed on the experimental platform, and the lower segment of the esophagus was clamped using an intestinal forceps. Then, a gastroscope (Xi'an Xichuan Medical Equipment Co., LTD.) was entered into the upper esophagus, and the esophagus was inflated properly to observe the air tightness and integrity of the esophageal mucosa. The esophageal mucosal lesions located locations are all located 10-15 cm from the beginning of the esophagus were marked using an electric knife (Nanwei Medical Technology Co., LTD.) through the gastroscopic operation hole. Then, the electric knife was retracted, and a soft tissue clip was inserted into the gastroscope operating hole and extended from the front end of the gastroscope. In the operational group, the TM was fixed on the soft tissue clip with a thin wire through the small hole at the end of the TM such that the opening and closing of the soft tissue clip were not affected. The gastroscope together with the soft tissue clip and the TM was delivered into the esophageal cavity, and the handle of the soft tissue clip was manipulated in a way that the TM and the soft tissue clip were fixed on the mucosa of the lesion. The AM was then slowly placed outside the esophagus on the other side of the mucosal lesion. Under gastroscopy, the TM was slowly sucked up by the AM. By changing the relative position of the magnets and the distance between the AM and TM, the traction direction of and the pulling force exerted on the TM can be adjusted to clearly display and assist the peeling of the pathological mucosa under endoscopy. The following parameters were evaluated in the two groups: The total operative time, perforation rate, rate of whole mucosal resection, diameter of the peering mucosa, and scores of endoscopists' feelings with the procedure, including the convenience, mucosal surface exposure degree, and tissue tension. To ensure comparability between the two groups, all ESD procedures in the study were performed by the same endoscopy resident.



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Figure 1 Physical drawing of the magnetic anchor device by us. A: The anchor magnet; B: The soft tissue clip and target magnet, and the connection of the two parts. AM: Anchor magnet; TM: Target magnet.



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Figure 2 Measurement of magnetic force-distance curve. A: The experiment of the measurement of the magnetic force-distance curve; B: The relationship between the separation of anchor magnet and target magnet and the magnetic force. AM: Anchor magnet; TM: Target magnet.

Statistical analysis

Qualitative data were expressed in terms of the number of actual cases (proportion, %), and comparisons of these data were performed using the χ^2 test. Quantitative data with normal distribution were expressed as mean \pm SD, and independent *t*-test was used to compare the two-group mean. Non-normally distributed data were expressed as median (interquartile interval), and a nonparametric test was used to compare the two groups. Statistical analysis was performed using IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY), with $P < 0.05$ indicating statistical significance.

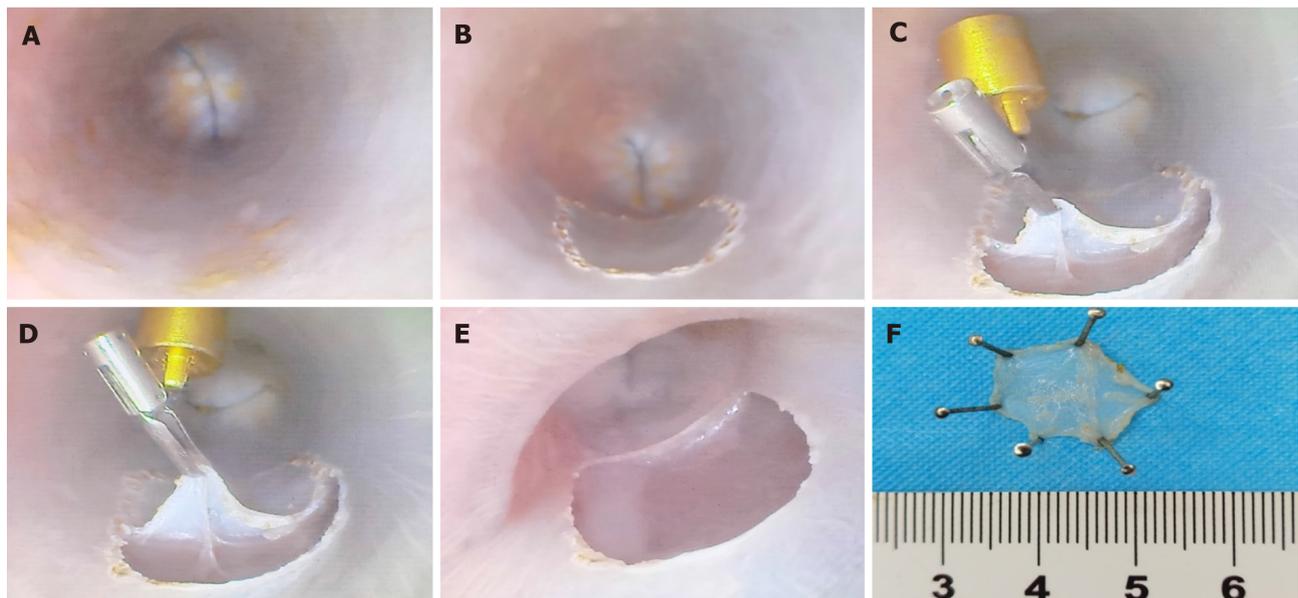
RESULTS

Operational process

The experiment involving the use of MAT-assisted ESD in isolated pig esophagi was successfully completed. After the gastroscope successfully entered the esophageal cavity before the operation, the isolated esophageal mucosa was visibly integral and light pink with good air tightness of the esophageal cavity (Figure 3A) and complete marking of the diseased mucosa (Figure 3B). In the operational group, with the help of gastroscopy, the soft tissue clip and the TM entered the isolated esophagus together. The connection between the two was firm, and the TM did not affect the opening, closing, or release of the soft tissue clip. At the same time, the soft tissue clip could smoothly clamp the esophageal mucosa without easily falling off (Figure 3C). When the AM was brought close to the other side of the pathological mucosa, the attraction between the AM and TM caused the TM to get pulled, thus exposing the mucosal dissection surface (Figure 3D). By slowly adjusting the position of the AM, the traction direction and tension of the TM could be changed to maintain good tissue tension on the surface of mucosal dissection and reduce the difficulty of mucosal dissection for the operator under the gastroscopy.

Operation time and operator score

The total operative times of the two groups were 17.04 and 21.94 min ($P < 0.001$), and the operational scores of endoscopists' feelings about the convenience (9.22 ± 0.19 vs 8.34 ± 0.15 , $P = 0.002$), mucosal surface exposure degree (9.11 ± 0.15



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Figure 3 The operational process of magnetic anchor technique-assisted endoscopic submucosal dissection. A: Esophageal mucosa was examined by gastroscopy; B: The putative diseased mucosa was marked with the electric knife; C and D: The target magnet and mucous membrane were sucked up, the operating field was exposed, and the direction and tissue tension were changed as the anchor magnet position was changed; E: The marked mucosa was completely exfoliated; F: The mucous membrane that has been removed.

vs 8.25 ± 0.12 , $P < 0.001$), and tissue tension (9.35 ± 0.13 *vs* 8.02 ± 0.17 , $P < 0.001$) were higher in the operational group than in the control group, indicating that MAT-assisted ESD could significantly shorten the operative time and improve the operating experience of endoscopists (Table 1). Finally, the mucosal surface was completely exfoliated (Figures 3E and F), and the diameters of the peering mucosa were 2.13 and 2.15 cm in the operational and control groups ($P = 0.882$).

Operation effect

There was one case of perforation and one case of incomplete mucosal resection in the operational group, and there were four cases of perforation and two cases of incomplete mucosal resection in the control group. There were no significant differences in the peering mucosa size, perforation rate, and rate of whole mucosal resection between the two groups (Table 1).

DISCUSSION

In this study, we determined that MAT-assisted ESD is a feasible and safe technique in an *in vitro* model. A magnetic anchor device designed by us was used to assist endoscopic esophageal submucosal dissection with special traction between the AM and TM. During the entire operation, the TM remained firmly connected to the soft tissue clip without affecting the opening and closing of the soft tissue clip. The TM was manipulated using the AM to expose the mucosal dissection surface and maintained the tissue tension of the mucosa. Figures 3C and D showed that the direction and tissue tension of the lesion mucosa pulled by the TM were changed after the AM position was changed. This helped the surgeon complete the operation, and no shedding of soft tissue clips or mucosal tearing occurred in the entire process. This assistive technology can greatly improve the operator's experience and shorten the operation time.

Magnetic surgery (MS) is an emerging surgical technique that uses the "non-contact" magnetic field force between magnets and uses specially designed magnetic devices to achieve several functions, such as cavity organ anastomosis and reconstruction as well as tissue and organ traction and exposure[26]. Currently, this is a clinical application system mainly comprising the magnetic compression technique, MAT, magnetic navigation technique, magnetic levitation technique, magnetic tracer technique, and magnetic drive technique[26]. MS has been implemented in gastrointestinal anastomosis reconstruction[27], vascular anastomosis reconstruction[28], and recanalization of biliary tract occlusion after liver transplantation[29]. Being one of the core clinical techniques of MS, MAT is a non-contact spatial anchor technique involving an AM and a TM which works *via* the magnetic attraction between magnets or of magnets with paramagnetic materials[26]. At present, MAT has been used in general surgery[30,31], gynecology[31,32], urology[33], and thoracic surgery[34]. In addition to the application of MAT in organ traction under laparoscopic and thoracoscopic surgeries, it has shown significant application in assisted endoscopic surgery as well[35].

A significant differentiating advantage of our research compared to other research on this subject is that we have optimized the structure of the TM. Because the TM is located in the digestive tract, the connection between the TM and the soft tissue clip needs to be considered in the design, and the volume of the TM should be minimized while ensuring it meets the magnetic requirements. In this study, we used magnetic shielding technology, wherein the magnetic attraction

Table 1 Comparison of results of the two groups

	Operational group (n = 10)	Control group (n = 10)	P value
Total operative time (min)	17.04 ± 0.22	21.94 ± 0.23	< 0.001
Perforation rate (%)	90	60	0.302
Rate of whole mucosal resection (%)	90	80	-
Diameters of the peering mucosa (cm)	2.13 ± 0.06	2.15 ± 0.06	0.822
Scores of convenience ¹	9.22 ± 0.19	8.34 ± 0.15	0.002
Scores of mucosal surface exposure degree ¹	9.11 ± 0.15	8.25 ± 0.12	< 0.001
Scores of tissue tension ¹	9.35 ± 0.13	8.02 ± 0.17	< 0.001

¹Endoscopist's operational feeling scores which were limited from 0 to 10 reflect their feelings about convenience, mucosal surface exposure degree, and tissue tension with the surgical procedure. Higher scores indicate greater satisfaction.

of the non-working surface could be significantly reduced by adding a permalloy shell to the TM to eliminate the interference of the TM during endoscopic operation. In addition, the tail hanging structure of the permalloy shell allows for a connection of the TM with the soft tissue clip. According to different anchor positions, MAT can be divided into external anchor technology and internal anchor technology, with both having different applications. This study uses the internal anchor technology, which provides endoscope-independent traction by primarily creating an invisible hand for the operator. Unlike other auxiliary methods, MAT-assisted ESD does not interfere with ESD operation and provides dynamic traction. Herein, the AM can be moved to manipulate the TM such that it exposes the mucosal dissection surface and provides the tissue tension required for endoscopic resection.

As an *in vitro* experiment, the condition of this experiment is different from those of internal animal experiments and clinical experiments. We could not assess the risk of postoperative complications, such as bleeding, perforation, and stenosis. Nevertheless, we believe that the results of this study lay a solid foundation for internal animal experiments, particularly in terms of the operation process, the precise control of the pulling direction, and the pulling force between the AM and the TM.

This study has some limitations. First, the operational group and control group had small sample sizes. Second, the ESD operators in this study were trainees in endoscopy technology, thus resulting in a higher perforation rate. However, we believe that this does not affect the comparisons with the operational group as the same operator worked with both operational and control groups. In addition, *in vitro* and *in vivo* organs have a greater difference, and the difficulty of ESD operation is significantly increased in *in vitro* organs, which is also a reason for the high perforation rate.

In vitro experiments have upheld the advantages of MAT in ESD. However, the technology still needs further advancements before it is ready for clinical use. In future studies, animal experiments should be conducted, and besides intraoperative complications, long-term postoperative incidence should also be observed. In addition, ways to optimize the magnetic anchor device, particularly to increase the flexibility of the use of AM, should also be explored in further research.

CONCLUSION

This experiment showed that MAT has significant advantages and can be used for endoscopic esophageal submucosal dissection. With the development of further internal animal experiments and the accumulation of operational experience, this technique has broad clinical application prospects.

ARTICLE HIGHLIGHTS

Research background

Esophageal cancer has high incidence and poor prognosis globally. Endoscopic submucosal dissection (ESD) has become the standard therapy for managing early tumors of the esophagus, stomach, and colon. However, there are some deficiencies, such as a steep learning curve, difficult operation, and technically demanding nature of the procedure. Magnetic anchor technique (MAT) is a brand new ESD assistance technique to improve the procedure of ESD.

Research motivation

Although ESD has become the golden treatment for early esophageal cancer, some limitations such as a steep learning curve and plenty of complications can still significantly improve. It already had some assisted techniques, which had trouble in controlling and maintaining tissue tension. The magnetic anchor device designed by our own is aspired to solve the problems mentioned above.

Research objectives

This study aims to testify the feasibility and safety of MAT-assisted ESD for early esophageal cancer.

Research methods

The experimental model used in this study was isolated pig esophagi, and the magnetic anchor device was designed by us, consisting of three parts: Target magnet (TM), anchor target (AM) and soft tissue clip. It was divided into two groups, namely the operational and control groups, and 10 endoscopists completed the procedure. In the operational group, the soft tissue clip together with the TM was connected by a thin wire through a small hole at the tail end of the TM, and was clamped to the edge of the lesioned mucosa, which was marked in advance. By changing the position of the AM outside the esophagus, the pulling force and pulling direction of the TM could be changed, thus exposing the mucosal peeling surface and assisting the ESD. The two groups were evaluated for the following aspects by SPSS: The total operative time, perforation rate, rate of whole mucosal resection, diameter of the peering mucosa, and scores of endoscopists' feelings with the procedure, including the convenience, mucosal surface exposure degree, and tissue tension.

Research results

The two groups did not significantly differ in the diameter of the peering mucosa, perforation rate and rate of whole mucosal resection. In the operational group, the TM remained firmly connected with the soft tissue clip and did not affect the opening, closing, and release of the soft tissue clip. The interaction between the TM and AM could provide sufficient tissue tension and completely expose the mucosa, which greatly assisted the endoscopists' feelings with the operation, which were higher in the operational group than in the control group in terms of the convenience (9.22 ± 0.19 vs 8.34 ± 0.15 , $P = 0.002$), mucosal surface exposure degree (9.11 ± 0.15 vs 8.25 ± 0.12 , $P < 0.001$), and tissue tension (9.35 ± 0.13 vs 8.02 ± 0.17 , $P < 0.001$). In addition, the total operative time was shorter in the operational group than in the control group.

Research conclusions

The MAT-assisted ESD was safe and feasible for early esophageal cancer.

Research perspectives

With the development of further internal animal experiments and the accumulation of operational experience, this technique has broad clinical application prospects.

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FOOTNOTES

Author contributions: Lyu Y and Yan XP conceived and designed the study; Pan M and Zhang MM performed the research and acquired the data; Xu SQ wrote the manuscript; Pan M and Zhang MM revised the manuscript; Lyu Y and Yan XP examined the final manuscript; and all authors read and approved the final manuscript.

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