ISSN 1948-5190 (online)

World Journal of *Gastrointestinal Endoscopy*

World J Gastrointest Endosc 2023 October 16; 15(10): 584-633

Published by Baishideng Publishing Group Inc

World Journal of Gastrointestinal Endoscopy

Contents

Monthly Volume 15 Number 10 October 16, 2023

ORIGINAL ARTICLE

Basic Study

Retrospective Cohort Study

Retrospective Study

CASE REPORT

World Journal of Gastrointestinal Endoscopy

Monthly Volume 15 Number 10 October 16, 2023

Contents

ABOUT COVER

Editorial Board Member of *World Journal of Gastrointestinal Endoscopy*, Mesut Akarsu, MD, Full Professor, Division of Gastroenterology, Department of Internal Medicine, Faculty of Medicine, Dokuz Eylul University, Izmir 35320, Turkey. mesut.akarsu@deu.edu.tr

AIMS AND SCOPE

The primary aim of *World Journal of Gastrointestinal Endoscopy* (*WJGE*, *World J Gastrointest Endosc*) is to provide scholars and readers from various fields of gastrointestinal endoscopy with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJGE mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal endoscopy and covering a wide range of topics including capsule endoscopy, colonoscopy, double-balloon enteroscopy, duodenoscopy, endoscopic retrograde cholangiopancreatography, endosonography, esophagoscopy, gastrointestinal endoscopy, gastroscopy, laparoscopy, natural orifice endoscopic surgery, proctoscopy, and sigmoidoscopy.

INDEXING/ABSTRACTING

The *WJGE* is now abstracted and indexed in Emerging Sources Citation Index (Web of Science), PubMed, PubMed Central, Reference Citation Analysis, China National Knowledge Infrastructure, China Science and Technology Journal Database, and Superstar Journals Database. The 2023 Edition of Journal Citation Reports® cites the 2022 impact factor (IF) for *WJGE* as 2.0; IF without journal self cites: 1.9; 5-year IF: 3.3; Journal Citation Indicator: 0.28.

RESPONSIBLE EDITORS FOR THIS ISSUE

NAME OF JOURNAL

World Journal of Gastrointestinal Endoscopy

ISSN

ISSN 1948-5190 (online)

LAUNCH DATE

October 15, 2009

FREQUENCY

Monthly

PUBLICATION DATE

October 16, 2023

World Journal of Gastrointestinal Endoscopy

Submit a Manuscript: https://www.f6publishing.com

World J Gastrointest Endosc 2023 October 16; 15(10): 584-592

DOI: 10.4253/wjge.v15.i10.584

ISSN 1948-5190 (online)

ORIGINAL ARTICLE

Basic Study

Magnetic anchor technique assisted endoscopic submucosal dissection for early esophageal cancer

Min Pan, Miao-Miao Zhang, Shu-Qin Xu, Yi Lyu, Xiao-Peng Yan

Specialty type: Gastroenterology and hepatology

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): B
Grade C (Good): 0
Grade D (Fair): D
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

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.

Citation: Pan M, Zhang MM, Xu SQ, Lyu Y, Yan XP. Magnetic anchor technique assisted endoscopic submucosal dissection for early esophageal cancer. *World J Gastrointest Endosc* 2023; 15(10): 584-592
URL: https://www.wjgnet.com/1948-5190/full/v15/i10/584.htm
DOI: https://dx.doi.org/10.4253/wjge.v15.i10.584

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

Transluminal 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

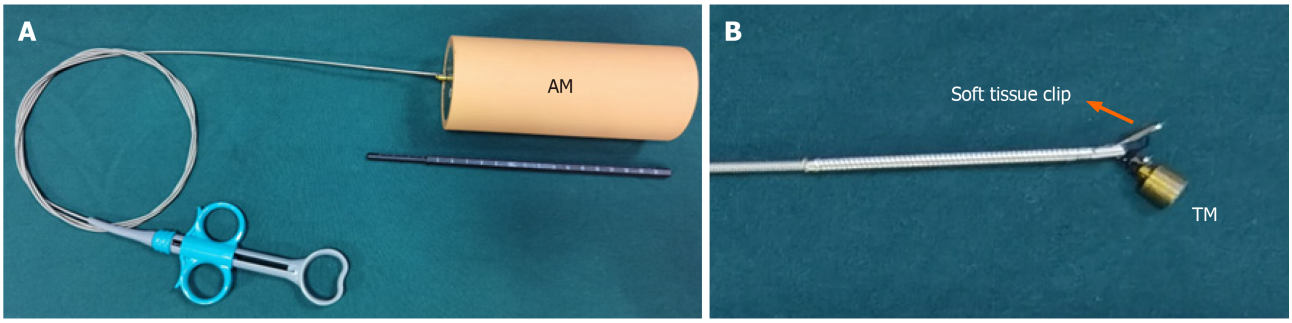
This was an *in vitro* animal experiment performed on isolated esophagi of 20 pigs divided into two groups, namely the operational group and control group. The pigs were obtained from the Experimental Animal Center of Xi'an Jiaotong University. We used the pigs that were euthanized by a professional 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).

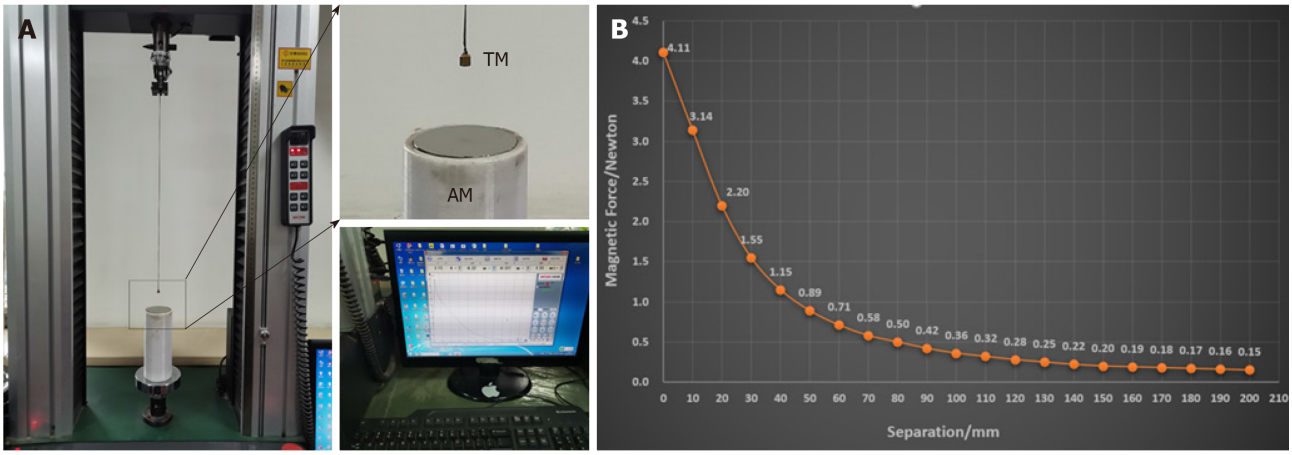
Operational process

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.



DOI: 10.4253/wjge.v15.i10.584 **Copyright** ©The Author(s) 2023.

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.



DOI: 10.4253/wjge.v15.i10.584 **Copyright** ©The Author(s) 2023.

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 ± 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.

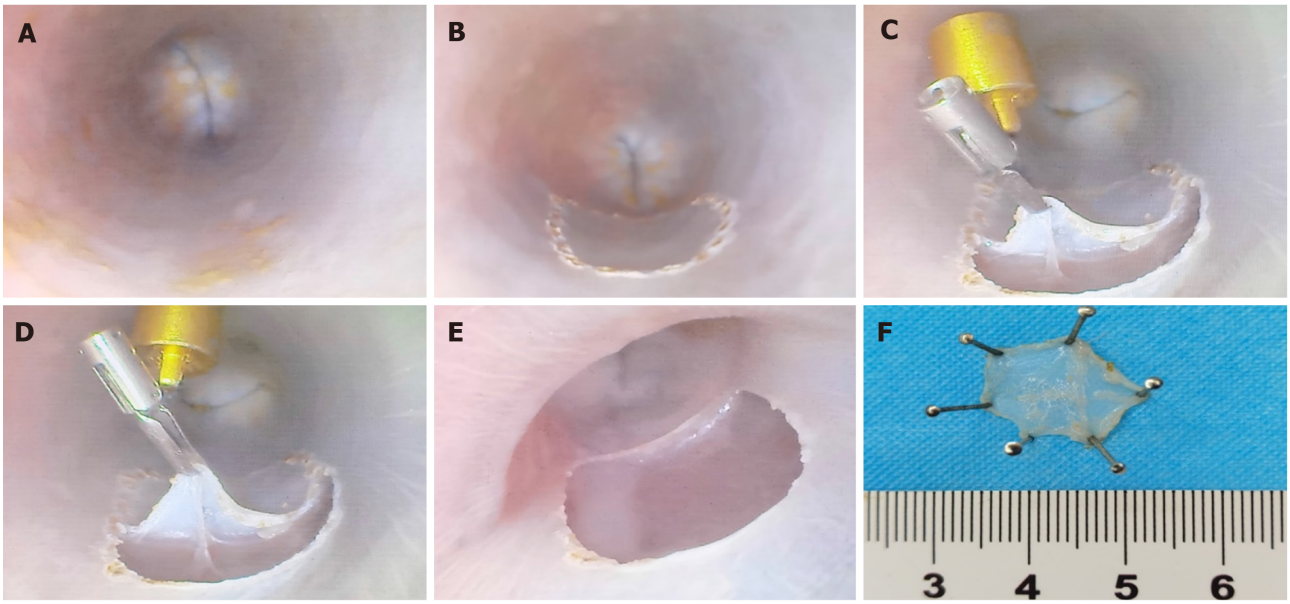
RESULTS

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



DOI: 10.4253/wjge.v15.i10.584

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

[1]Endoscopist'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.

ACKNOWLEDGEMENTS

We appreciated all individuals who participated in or helped with this research project.

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.

Supported by the Key Research & Development Program-Social Development of Shaanxi Province of China, No. 2021SF-163; and the Innovation Capability Support Plan of Shaanxi Province of China, No. 2020KJXX-022.

Institutional animal care and use committee statement: All animal experiments conformed to the internationally accepted principles for the laboratory animal care committee of Xi'an Jiaotong University (approval NO. XJTULAC2019-1006) and were in accordance with the ethical standards for experimental animals of Xi'an Jiaotong University.

Conflict-of-interest statement: All the authors report no relevant conflicts of interest for this article.

Data sharing statement: No additional data are available.

ARRIVE guidelines statement: The authors have read the ARRIVE guidelines, and the manuscript was prepared and revised according to the ARRIVE guidelines.

Country/Territory of origin: China

ORCID number: Min Pan 0000-0003-3381-3676; Miao-Miao Zhang 0000-0001-5679-7061; Shu-Qin Xu 0000-0002-1035-2750; Yi Lyu 0000-0003-3636-6664; Xiao-Peng Yan 0000-0002-0335-829X.

S-Editor: Wang JJ
L-Editor: A
P-Editor: Wang JJ

REFERENCES

1 **Sung H**, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin* 2021; **71**: 209-249 [PMID: 33538338 DOI: 10.3322/caac.21660]
2 **Ciocirlan M**, Lapalus MG, Hervieu V, Souquet JC, Napoléon B, Scoazec JY, Lefort C, Saurin JC, Ponchon T. Endoscopic mucosal resection for squamous premalignant and early malignant lesions of the esophagus. *Endoscopy* 2007; **39**: 24-29 [PMID: 17252456 DOI: 10.1055/s-2006-945182]
3 **Merkow RP**, Bilimoria KY, Keswani RN, Chung J, Sherman KL, Knab LM, Posner MC, Bentrem DJ. Treatment trends, risk of lymph node metastasis, and outcomes for localized esophageal cancer. *J Natl Cancer Inst* 2014; **106** [PMID: 25031273 DOI: 10.1093/jnci/dju133]
4 **Uhlenhopp DJ**, Then EO, Sunkara T, Gaduputi V. Epidemiology of esophageal cancer: update in global trends, etiology and risk factors. *Clin J Gastroenterol* 2020; **13**: 1010-1021 [PMID: 32965635 DOI: 10.1007/s12328-020-01237-x]
5 **Mortagy M**, Mehta N, Parsi MA, Abe S, Stevens T, Vargo JJ, Saito Y, Bhatt A. Magnetic anchor guidance for endoscopic submucosal dissection and other endoscopic procedures. *World J Gastroenterol* 2017; **23**: 2883-2890 [PMID: 28522906 DOI: 10.3748/wjg.v23.i16.2883]
6 **Yang D**, Othman M, Draganov PV. Endoscopic Mucosal Resection *vs* Endoscopic Submucosal Dissection For Barrett's Esophagus and Colorectal Neoplasia. *Clin Gastroenterol Hepatol* 2019; **17**: 1019-1028 [PMID: 30267866 DOI: 10.1016/j.cgh.2018.09.030]
7 **Landin MD**, Guerrón AD. Endoscopic Mucosal Resection and Endoscopic Submucosal Dissection. *Surg Clin North Am* 2020; **100**: 1069-1078 [PMID: 33128880 DOI: 10.1016/j.suc.2020.07.004]
8 **Chandrasekhara V**, Sigmon JC Jr, Surti VC, Kochman ML. A novel gel provides durable submucosal cushion for endoscopic mucosal resection and endoscopic submucosal dissection. *Surg Endosc* 2013; **27**: 3039-3042 [PMID: 23392984 DOI: 10.1007/s00464-013-2813-y]
9 **Repici A**. Endoscopic submucosal dissection: established, or still needs improving? *Gastrointest Endosc* 2009; **69**: 16-18 [PMID: 19111684 DOI: 10.1016/j.gie.2008.07.030]
10 **Fukami N**. What we want for ESD is a second hand! Traction method. *Gastrointest Endosc* 2013; **78**: 274-276 [PMID: 23867374 DOI: 10.1016/j.gie.2013.04.192]
11 **Kobayashi T**, Gotohda T, Tamakawa K, Ueda H, Kakizoe T. Magnetic anchor for more effective endoscopic mucosal resection. *Jpn J Clin Oncol* 2004; **34**: 118-123 [PMID: 15078906 DOI: 10.1093/jjco/hyh025]
12 **Ahmed Y**, Othman M. EMR/ESD: Techniques, Complications, and Evidence. *Curr Gastroenterol Rep* 2020; **22**: 39 [PMID: 32542462 DOI: 10.1007/s11894-020-00777-z]
13 **Oyama T**. Counter traction makes endoscopic submucosal dissection easier. *Clin Endosc* 2012; **45**: 375-378 [PMID: 23251884 DOI: 10.5946/ce.2012.45.4.375]
14 **Lee BI**. Debates on colorectal endoscopic submucosal dissection - traction for effective dissection: gravity is enough. *Clin Endosc* 2013; **46**: 467-471 [PMID: 24143304 DOI: 10.5946/ce.2013.46.5.467]
15 **Kondo H**, Gotoda T, Ono H, Oda I, Kozu T, Fujishiro M, Saito D, Yoshida S. Percutaneous traction-assisted EMR by using an insulation-tipped electrosurgical knife for early stage gastric cancer. *Gastrointest Endosc* 2004; **59**: 284-288 [PMID: 14745409 DOI: 10.1016/s0016-5107(03)02533-1]
16 **Saito Y**, Emura F, Matsuda T, Uraoka T, Nakajima T, Ikematsu H, Gotoda T, Saito D, Fujii T. A new sinker-assisted endoscopic submucosal dissection for colorectal cancer. *Gastrointest Endosc* 2005; **62**: 297-301 [PMID: 16046999 DOI: 10.1016/s0016-5107(05)00546-8]
17 **Motohashi O**, Nishimura K, Nakayama N, Takagi S, Yanagida N. Endoscopic submucosal dissection (two-point fixed ESD) for early esophageal cancer. *Dig Endosc* 2009; **21**: 176-179 [PMID: 19691765 DOI: 10.1111/j.1443-1661.2009.00881.x]
18 **Ritsuno H**, Sakamoto N, Osada T, Goto SP, Murakami T, Ueyama H, Mori H, Matsumoto K, Beppu K, Shibuya T, Nagahara A, Ogihara T, Watanabe S. Prospective clinical trial of traction device-assisted endoscopic submucosal dissection of large superficial colorectal tumors using the S-O clip. *Surg Endosc* 2014; **28**: 3143-3149 [PMID: 24879138 DOI: 10.1007/s00464-014-3572-0]
19 **Matsumoto K**, Nagahara A, Ueyama H, Konuma H, Morimoto T, Sasaki H, Hayashi T, Shibuya T, Sakamoto N, Osada T, Ogihara T, Yao T, Watanabe S. Development and clinical usability of a new traction device "medical ring" for endoscopic submucosal dissection of early gastric cancer. *Surg Endosc* 2013; **27**: 3444-3451 [PMID: 23525882 DOI: 10.1007/s00464-013-2887-6]
20 **Ho KY**, Phee SJ, Shabbir A, Low SC, Huynh VA, Kencana AP, Yang K, Lomanto D, So BY, Wong YY, Chung SC. Endoscopic submucosal dissection of gastric lesions by using a Master and Slave Transluminal Endoscopic Robot (MASTER). *Gastrointest Endosc* 2010; **72**: 593-599 [PMID: 20646698 DOI: 10.1016/j.gie.2010.04.009]
21 **Diana M**, Chung H, Liu KH, Dallemagne B, Demartines N, Mutter D, Marescaux J. Endoluminal surgical triangulation: overcoming challenges of colonic endoscopic submucosal dissections using a novel flexible endoscopic surgical platform: feasibility study in a porcine model. *Surg Endosc* 2013; **27**: 4130-4135 [PMID: 23793807 DOI: 10.1007/s00464-013-3049-6]
22 **Fujii L**, Onkendi EO, Bingener-Casey J, Levy MJ, Gostout CJ. Dual-scope endoscopic deep dissection of proximal gastric tumors (with video). *Gastrointest Endosc* 2013; **78**: 365-369 [PMID: 23394839 DOI: 10.1016/j.gie.2012.12.010]
23 **Kobiela J**, Grymek S, Wojanowska M, Lubniewski M, Makarewicz W, Dobrowolski S, Lachiński AJ, Sledziński Z. Magnetic instrumentation and other applications of magnets in NOTES. *Wideochir Inne Tech Maloinwazyjne* 2012; **7**: 67-73 [PMID: 23256005 DOI: 10.5114/wiitm.2011.25665]
24 **Gotoda T**, Oda I, Tamakawa K, Ueda H, Kobayashi T, Kakizoe T. Prospective clinical trial of magnetic-anchor-guided endoscopic submucosal dissection for large early gastric cancer (with videos). *Gastrointest Endosc* 2009; **69**: 10-15 [PMID: 18599053 DOI: 10.1016/j.gie.2008.03.1127]
25 **Matsuzaki I**, Hattori M, Yamauchi H, Goto N, Iwata Y, Yokoi T, Tsunemi M, Kobayashi M, Yamamura T, Miyahara R. Magnetic anchor-guided endoscopic submucosal dissection for colorectal tumors (with video). *Surg Endosc* 2020; **34**: 1012-1018 [PMID: 31571035 DOI: 10.1007/s00464-019-07127-9]

26 **Yan XP**, Shang P, Shi AH, Liu WY, Liu YX, Lv Y. [Exploration and establishment of magnetic surgery]. *Chin Sci Bull* 2019; 815-826

27 **An Y**, Zhang Y, Liu H, Ma S, Fu S, Lv Y, Yan X. Gastrojejunal anastomosis in rats using the magnetic compression technique. *Sci Rep* 2018; **8**: 11620 [PMID: 30072707 DOI: 10.1038/s41598-018-30075-8]

28 **Wang HH**, Ma J, Wang SP, Ma F, Lu JW, Xu XH, Lv Y, Yan XP. Magnetic Anastomosis Rings to Create Portacaval Shunt in a Canine Model of Portal Hypertension. *J Gastrointest Surg* 2019; **23**: 2184-2192 [PMID: 30132290 DOI: 10.1007/s11605-018-3888-5]

29 **Li Y**, Sun H, Yan X, Wang S, Dong D, Liu X, Wang B, Su M, Lv Y. Magnetic compression anastomosis for the treatment of benign biliary strictures: a clinical study from China. *Surg Endosc* 2020; **34**: 2541-2550 [PMID: 31399950 DOI: 10.1007/s00464-019-07063-8]

30 **Cho YB**, Park CM, Chun HK, Yi LJ, Park JH, Yun SH, Kim HC, Lee WY. Transvaginal endoscopic cholecystectomy using a simple magnetic traction system. *Minim Invasive Ther Allied Technol* 2011; **20**: 174-178 [PMID: 21417833 DOI: 10.3109/13645706.2010.526911]

31 **Shang Y**, Guo H, Zhang D, Xue F, Yan X, Shi A, Dong D, Wang S, Ma F, Wang H, Li J, Liu X, Luo R, Wu R, Lv Y. An application research on a novel internal grasper platform and magnetic anchoring guide system (MAGS) in laparoscopic surgery. *Surg Endosc* 2017; **31**: 274-280 [PMID: 27177955 DOI: 10.1007/s00464-016-4968-9]

32 **Padilla BE**, Dominguez G, Millan C, Martinez-Ferro M. The use of magnets with single-site umbilical laparoscopic surgery. *Semin Pediatr Surg* 2011; **20**: 224-231 [PMID: 21968159 DOI: 10.1053/j.sempedsurg.2011.05.007]

33 **Choi YH**, Lee HW, Lee SY, Han DH, Seo SI, Jeon SS, Lee HM, Choi HY, Jeong BC. Laparoendoscopic single-site simple nephrectomy using a magnetic anchoring system in a porcine model. *Investig Clin Urol* 2016; **57**: 208-214 [PMID: 27195320 DOI: 10.4111/icu.2016.57.3.208]

34 **Gonzalez-Rivas D**. Unisurgeon' uniportal video-assisted thoracoscopic surgery lobectomy. *J Vis Surg* 2017; **3**: 163 [PMID: 29302439 DOI: 10.21037/jovs.2017.10.07]

35 **Bai JG**, Wang Y, Zhang Y, Lv Y; Scientific Committee of the Third International Conference of Magnetic Surgery. Expert consensus on the application of the magnetic anchoring and traction technique in thoracoscopic and laparoscopic surgery. *Hepatobiliary Pancreat Dis Int* 2022; **21**: 7-9 [PMID: 34289952 DOI: 10.1016/j.hbpd.2021.06.007]

World Journal of Gastrointestinal Endoscopy

Submit a Manuscript: https://www.f6publishing.com

World J Gastrointest Endosc 2023 October 16; 15(10): 593-601

DOI: 10.4253/wjge.v15.i10.593

ISSN 1948-5190 (online)

ORIGINAL ARTICLE

Retrospective Cohort Study

Direct cost variance analysis of peroral endoscopic myotomy *vs* heller myotomy for management of achalasia: A tertiary referral center experience

Syedreza Ali Haider, Gregory S Bills, C Prakash Gyawali, Passisd Laoveeravat, Jordan Miller, Samir Softic, Mihir S Wagh, Moamen Gabr

Specialty type: Gastroenterology and hepatology

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): 0
Grade C (Good): C
Grade D (Fair): D, D
Grade E (Poor): 0

P-Reviewer: Costantini M, Italy; Wang ZK, China

Received: July 6, 2023
Peer-review started: July 6, 2023
First decision: August 4, 2023
Revised: August 23, 2023
Accepted: September 11, 2023
Article in press: September 11, 2023
Published online: October 16, 2023

Syedreza Ali Haider, Department of Internal Medicine, Washington University School of Medicine St. Louis, St. Louis, MO 63018, United States

Gregory S Bills, Passisd Laoveeravat, Department of Digestive Disease and Nutrition, University of Kentucky College of Medicine, Lexington, KY 40508, United States

C Prakash Gyawali, Department of Internal Medicine, Washington University School of Medicine St. Louis and Barnes Jewish Hospital, St. Louis, MO 63108, United States

Jordan Miller, Department of Cardiothoracic Surgery, University of Kentucky College of Medicine, Lexington, KY 40508, United States

Samir Softic, Department of Pediatrics, University of Kentucky College of Medicine and Kentucky Children's Hospital, Lexington, KY 40508, United States

Mihir S Wagh, Interventional Endoscopy, Division of Gastroenterology, University of Colorado School of Medicine, Aurora, CO 80045, United States

Moamen Gabr, Department of Advanced Endoscopy, Beth Israel Deaconess Medical Center, Boston, MA 02215, United States

Corresponding author: Moamen Gabr, FASGE, MD, MSc, Director, Department of Advanced Endoscopy, Beth Israel Deaconess Medical Center, 330 Brookline Avenue, Dana 501, Boston, MA 02215, United States. mgabr@bidmc.harvard.edu

Abstract

BACKGROUND

Laparoscopic Heller myotomy (LHM) has been the traditional surgical treatment for achalasia. Recently, peroral endoscopic myotomy (POEM) has demonstrated similar clinical outcomes with shorter procedure times. Studies comparing the direct cost-effectiveness of POEM *vs* LHM are limited.

AIM

To compare costs of POEM *vs* LHM.

METHODS

This retrospective chart review aimed to compare the outcomes and cost of clinical care between patients who underwent POEM and LHM procedures for achalasia. The study was conducted at a tertiary academic center from January 2019 to December 2020. Clinical outcomes, including post-operative Eckardt scores and adverse events, were assessed and compared between the two groups. Direct cost variance analysis was utilized to evaluate the cost of clinical care incurred by patients undergoing POEM in the year preceding the procedure, during the index admission, and one year post-procedure, in comparison to patients undergoing LHM.

RESULTS

Of 30 patients were included (15 POEM and 15 LHM) in the study. Patients in the POEM group had a mean Eckardt score of 0.5 ± 0.5 post-procedure, which was no different from patients in the LHM group (0.7 ± 0.6, P = 0.17) indicating comparative efficacy. However, the total costs of the admission for the procedure in the LHM group were on average $1827 more expensive than in the POEM group (P < 0.01). Total healthcare costs one year prior to index procedure were $7777 higher in the LHM group, but not statistically different (P = 0.34). The patients in the LHM group one year after the index procedure had accrued $19730.24 larger total cost, although this was not statistically different from POEM group (P = 0.68).

CONCLUSION

Despite similar clinical outcomes, the cost of the index procedure admission for POEM was significantly lower than for LHM. The difference was primarily related to shorter time increments utilized in the operating room during the index procedure, and shorter length of hospital stay following POEM.

Key Words: Peroral endoscopic myotomy; Cost analysis; Laparoscopic Heller myotomy; Achalasia

Core Tip: This manuscript focuses on comparing the clinical outcomes and costs of laparoscopic Heller myotomy (LHM) and peroral endoscopic myotomy (POEM) as treatment options for achalasia, a rare esophageal motility disorder. Achalasia is characterized by impaired relaxation of the lower esophageal sphincter and abnormal peristalsis in the esophageal body, resulting in symptoms such as dysphagia, regurgitation, chest pain, and weight loss. The study aims to determine the clinical efficacy and cost-effectiveness of both procedures. By analyzing data from a tertiary-academic referral center, the researchers investigate the clinical outcomes, costs prior to and following the procedure, and adverse events associated with LHM and POEM.

Citation: Haider SA, Bills GS, Gyawali CP, Laoveeravat P, Miller J, Softic S, Wagh MS, Gabr M. Direct cost variance analysis of peroral endoscopic myotomy *vs* heller myotomy for management of achalasia: A tertiary referral center experience. *World J Gastrointest Endosc* 2023; 15(10): 593-601

URL: https://www.wjgnet.com/1948-5190/full/v15/i10/593.htm

DOI: https://dx.doi.org/10.4253/wjge.v15.i10.593

INTRODUCTION

Achalasia is a rare, idiopathic esophageal motility disorder characterized by impaired relaxation of the lower esophageal sphincter (LES) and abnormal smooth muscle peristalsis in the esophageal body[1-3]. Typical symptoms consist of dysphagia, regurgitation of food from the esophagus, chest pain and weight loss, resulting from incomplete transfer of nutrients past the LES[2,4,5]. Definitive management requires disruption of the obstructive LES, traditionally performed endoscopically as pneumatic dilation (PD) or surgically as laparoscopic Heller myotomy (LHM)[2]. More recently, peroral endoscopic myotomy (POEM) has become available with increasing utilization in the last decade[3,6,7]. Clinical success was similar between patients undergoing either procedure at two years, however, serious adverse events were more frequent in patients undergoing LHM with acid reflux being a more common symptoms in patients undergoing POEM[6].

Considering that escalating healthcare costs represent a large economic burden to the patients and society, comparative cost-effectiveness may be the eventual driver of which management option is a preferred treatment option. The aim of this study was to compare clinical outcomes, costs one-year prior to the procedure, during the index admission, and one-year after the procedure between LHM and POEM at a tertiary-academic referral center where both options were available.

MATERIALS AND METHODS

Data source and population

Clinical data was obtained retrospectively from chart review of the University of Kentucky Medical Center electronic medical record (EMR). Cases were identified by interrogating the EMR for adult patients (age > 18 years) with dysphagia and achalasia based on International Classification of Diseases-10 (ICD-10) codes (K22.0, R13.10), and abstracting all patients treated with POEM or LHM between January 2019 and December 2020. Patients with prior foregut surgery, patients without manometrically confirmed achalasia, and those without healthcare encounters at our hospital system one year before and after the index procedure were excluded. Sixteen patients underwent POEM and another sixteen subjects had LHM within the same timeframe (maximum 24-mo interval) to minimize cost variability over time. POEM was performed by a trained interventional endoscopist who performed at least 20 procedures prior to the study period and LHM was performed by a trained cardiothoracic surgeon who performed at least 20 procedures prior to the study period. The decision to undergo either POEM or LHM and thus allocation to either group was a function of insurance coverage, patient preference, and provider type (gastroenterologist or surgeon) and was performed without randomization. Given the retrospective nature of the study, the full logic behind allocation was influenced by various factors and could not be fully detailed due to the complexity and individualized nature of patient decision-making processes. The finance office at our institution provided cost data for each procedure.

The study protocol and data analysis described was approved by the University of Kentucky Institutional Review Board (IRB). A waiver of informed consent was granted as the study retrospectively evaluated de-identified data. All data security safeguards were strictly followed as per IRB policy.

LHM and POEM protocol

Pre-operative protocol for both LHM and POEM were similar. All patients in both groups underwent pre-procedural esophagram, esophagogastroduodenoscopy (EGD) to rule out pseudo-achalasia, diagnosis with manometry study, pre-operative clinical visits with the performing endoscopist or surgeon, as well as a pre-operative anesthesia visit.

The procedure technique employed for both LHM and POEM have been described elsewhere[8,9]. All patients in the LHM group underwent Dor or Toupet fundoplication. General anesthesia was used for all cases, and all patients were subsequently admitted for at least one night for post-op recovery and observation. All POEM procedures were performed in the operating room (OR). Procedural technique for POEM involved a mix of anterior and posterior approaches. All patients were scheduled at the 1, 6, and 12 mo time points in clinic for follow up, and all were evaluated with post-operative gastrografin study to evaluate for leak. Follow up EGD, manometry and pH studies were performed dependent on patient symptomatology and recovery.

Variables and outcomes

For the patients in the study, clinical variables were extracted from review of EMR. Demographic information, disease characteristics (subtype of achalasia, duration of symptoms, symptomatology, previous therapies), and intervention-related variables (efficacy: Pre- and post-intervention Eckardt score, length of stay for the index procedure, complications, readmission, time to last follow up visit) were extracted. Eckardt score was calculated as a total score of four symptom components: Dysphagia, regurgitation, chest pain, and weight loss, on 4 point Likert scales (0 = none, 3 = with every meal or severe)[10]. Costs incurred were reviewed from one year prior to index procedure, during index admission, and one-year post-procedure. Clinical success was defined as Eckardt score < 3 after POEM or LHM. Procedure related adverse events were recorded and categorized per published American Society for Gastrointestinal Endoscopy criteria[11]. Adverse events were identified by chart review, including clinical encounters, index and subsequent hospitalizations, as well as ER visits at our institution within one year of the index admission.

Cost data collection

Due to variance in reimbursement rates, we elected to use healthcare charges as a surrogate for the cost for each patient. All achalasia-related charges billed by the institution's hospital network system were obtained for one-year prior to the index admission, the index procedure admission, and one-year following the index admission. Costs derived from achalasia diagnosis and management were identified by manual review of each medical charge for both inpatient and outpatient encounters. This review was conducted by one of the study authors (Haider SA) for the period one-year prior and one year following the procedure. In addition to encounters with ICD-10 codes K22.0 "Achalasia of Esophagus" and R13.10 "Dysphagia Unspecified", other medical encounters with diagnoses including to A41.9 "Sepsis, Unspecified Organism", K22.5 "Diverticulum of Esophagus Acquired", R11.10 "Vomiting Unspecified", R07.89 "Other Chest Pain", J18.9 " pneumonia", and J90.0 "pleural effusion" were reviewed to determine the relationship to the index procedure. ICD codes were selected based on previous literature, to capture costs of the most commonly encountered adverse events related to the index procedure[12]. Encounters included ER visits, pre-surgical anesthesia evaluations, gastroenterology clinic visits, subsequent testing for monitoring of symptoms, primary care visits, and inpatient admissions were independently reviewed to determine relationship to the index procedure. Temporality to the index procedure, existing medical comorbidities, laboratory/imaging data, and provider assessment notes were considered in determining whether each healthcare encounter was attributable to the index procedure. Encounters unrelated to achalasia or the index procedure were excluded from the analysis.

The admission charge categories included anesthesia, electrocardiographic/telemetry, laboratory, surgical supplies, OR services (labor), time spent in intensive care unit (ICU)/observation, ancillary services, cardiac services, other specialty diagnostic services, other surgical services, pharmacy and intravenous therapy, physical therapy, respiratory

therapy services, inpatient accommodations, and radiology. A detailed breakdown of each cost category and associated charges can be found in Supplementary Table 1.

Statistical analysis

Means and standard deviations (SD) are the main statistical parameters in the analysis. Pearson χ^2 and Fisher's exact tests were used as appropriate to analyze the association between categorical variables. Two sample *t*-tests were used to compare independent continuous variables. To apply the two-tailed *t*-test, *F*-test for comparing the variances of two groups was used to determine if the two groups had equal variances. Paired *t*-tests were used to compare dependent variables. Confidence intervals are described as means ± one standard error. Total direct cost variance was calculated by totaling each charge category and then calculating the difference between the POEM and LHM group. Average cost variance was determined by calculating the mean for each charge category in the POEM and LHM group and then calculating the difference. The level of statistical significance used was 0.05. All analyses pag were performed in R version 3.6.3. The statistical methods of this study were reviewed Doaa Ali, MD, PhD, from the University of Kentucky.

RESULTS

Baseline characteristics

Of 30 patients, (mean age 54.2 and 52.6 in POEM and LHM group, respectively) were included in the study (15 underwent POEM and 15 LHM). Two patients, one who underwent LHM and one who underwent POEM in the study period, were excluded due to a lack of follow up and having undergone previous foregut surgery. Baseline characteristics including age, gender and weight were similar in the LHM and POEM cohorts ($P \geq 0.7$) (Table 1). Additionally, duration of symptoms ($P = 0.78$), achalasia subtypes ($P = 0.7$), proportions with prior botulinum toxin injection ($P = 0.7$) or PD ($P = 1.0$) as well as symptom severity as measured by the Eckardt score ($P = 0.24$), and symptoms score >2 ($P \geq 0.7$) were similar in both groups.

Clinical outcomes

Clinical success was seen in 15/15, 100% with POEM and in 14/15, 93% after LHM ($P = 0.98$). Post-procedure Eckardt score decreased from 7.0 (± 2.9) to 0.5 (± 0.5) in POEM group and from 5.8 (± 2.6) to 0.7 (± 0.6) in LHM group (Table 1). There was no statistically significant difference between the groups ($P = 0.17$) (Table 2), indicating that both procedures were equally effective in improving achalasia symptoms. Mean procedure time (range) was 82.3 min (66 min to 172 min) for POEM and 183 min (145 to 342 min) for LHM, $P = 0.02$. Adverse events occurred in 2/15, 13.3.% with POEM and in 4/15, 26.6% after LHM, ($P = 0.65$). Severe (serious) adverse events were experienced in one patient in the POEM group, and in one patient in the LHM group. One patient in both groups required a subsequent ICU stay. Though numerically higher in the LHM group, adverse events and readmission rates were statistically similar ($P \geq 0.6$) between the two groups. Adverse events in the LHM group ($n = 4$) included urinary retention, nausea and vomiting, unexplained diarrhea, aspiration pneumonia with sepsis; one patient with sepsis succumbed to illness. Adverse events in the POEM group ($n = 2$) included pneumomediastinum, and aspiration pneumonia with resultant lung abscess requiring thoracotomy. The patient requiring thoracotomy and lung abscess required 2 d in the ICU, however, was able to go home on IV antibiotics and subsequently recovered. Length of stay was significantly longer in the LHM group (2.26 ± 0.6 d) compared to the POEM group (1.1 ± 0.3 d, $P < 0.01$), and this was partly driven by a prolonged hospital stay associated with aspiration pneumonia and sepsis in one patient.

Costs

The average admission cost following LHM was $1828 more expensive than for POEM group ($P < 0.01$, Table 3). The majority of the cost difference were accounted by OR services, which were $545 higher ($P < 0.01$) per case in the LHM group. The other significant areas of cost difference between LHM and POEM were time spent in ICU/observation ($185), pharmacy and IV therapy ($124), and physical therapy ($15) ($P \leq 0.03$ for each comparison). The X-ray costs were more expensive with POEM group ($P < 0.01$). Anesthesia costs tended to be $88 per case higher in the LHM group *vs* the POEM group ($P = 0.05$). The LHM group required 10.2 additional 15 min unit charges on average for anesthesia, while the POEM group required 5.2 additional 15 min unit charges (Supplementary Table 1). Other comparisons did not demon-strate significant differences (Table 3). The patients had no difference in cost 1 year prior to index procedure ($P = 0.34$), and there was no difference in cost 1 year after the index procedure ($P = 0.68$).

DISCUSSION

Over the last decade numerous studies have shown the efficacy of POEM independently and in comparison to LHM for management of achalasia, with similar dysphagia improvement and patient-reported satisfaction[3,13,14]. Since cost of the therapy is another key metric when two therapies are assessed, we compared the index admission costs, as well as costs 1 year prior and 1 year following the procedure between patients undergoing LHM and POEM at a tertiary care center. We demonstrate that the cost of index admission for the procedure is significantly less expensive in patients undergoing POEM compared to LHM, despite similar costs during the year leading up to the procedure, as well as during the year following the procedure. The procedure related costs and duration of hospital stay also favored POEM

Table 1 Baseline characteristics of peroral endoscopic myotomy and laparoscopic Heller myotomy patients at time of intervention

	POEM (*n* = 15)	LHM (*n* = 15)	*P* value
Mean age in years (SD)	54.2 (8.6)	52.6 (7.3)	0.74
Gender (% female)	53	53	1.0
Mean weight (lbs, standard deviation)	183.3 (47)	188.4 (25.3)	0.26
Mean duration of symptoms (yr, SD)	7.1 (6.8)	7.3 (7.1)	0.78
Achalasia subtype[1]	4/7/3/1	4/8/1/2	0.70
Prior botulinum toxin	4	3	0.70
Pneumatic dilation	7	7	1.0
Mean Eckardt score (SD)	7.0 (2.9)	5.8 (2.6)	0.25
Symptom Score > 2, %			
Weight loss	67	73	1
Dysphagia	73	73	1
Regurgitation	67	80	0.67
Chest pain	20	20	1

[1]Type 1/type 2/type 3/hypercontractile esophagus.
POEM: Peroral endoscopic myotomy; LHM: Laparoscopic Heller myotomy.

Table 2 Patient outcomes following peroral endoscopic myotomy and laparoscopic Heller myotomy

	POEM (*n* = 15)	LHM (*n* = 15)	*P* value
Post-procedure Eckardt Scores mean (SD)	0.5 (0.5)	0.7 (0.6)	0.17
Adverse events (*n*, %)	2, 13.3%	4, 26.7%	0.65
Readmission rate (% of patients with readmission within one year)	6.7%	20.0%	0.59
LOS mean days (SD)	1.1 (0.3)	2.26 (0.6)	< 0.01[a]

[a]Denotes statistical significance at *P*-value < 0.05.
LOS: Length of stay; POEM: Peroral endoscopic myotomy; LHM: Laparoscopic Heller myotomy.

over LHM, with similar symptom resolution and patient outcomes, further supporting use of POEM as a standard option in the management of achalasia. It is important to underscore that the primary objective of this study was to juxtapose short-term costs within the post-procedure timeframe, while acknowledging the need for subsequent research to delve into the divergence of costs over a longer-term horizon (exceeding 1 year).

Previous cost-effectiveness analyses have favored endoscopic management options, such as PD demonstrating lower costs and better cost-effectiveness compared to LHM[6,15]. Prior cost-effectiveness analysis demonstrated similar rates between LHM and POEM[15]. In this study, Miller *et al*[15] report that POEM costs 1.058 times the cost of LHM, primarily since POEM was assigned a higher cost per minute of OR and anesthesia time, despite the fact that POEM procedures are less complex for the OR team. The increased cost per minute of POEM was attributed to POEM being an investigational procedure in the study design requiring IRB approval[15]. In our study, POEM was not considered investigational which could explain the lower costs. Greenleaf *et al*[6] conducted a cost-utility analysis and found similar costs in the index admission of patients undergoing POEM *vs* LHM ($8630 ± $2653 *vs* $7604 ± $2091), with no difference in mean QALYs. However, at a willingness-to-pay threshold of $100000, there was a 68.31% probability that POEM was cost-effective relative to LHM[6]. Furthermore, a recent Brazilian cost-utility study performed utilizing a bottom-up cost analysis found POEM to cost twice as much in the interoperative period *vs* LHM[11]. This was explained by the authors to be secondary to the disposable nature of endoscopic materials, and the use of depreciated equipment[16]. However, institution-dependent variables limit the generalizability of this evidence, hence comparisons incorporating non-operative costs and various institutional per unit costs was deemed necessary to further understand the cost differences and cost-effectiveness.

In our study, costs from procedure-related admission were on average $1828 less expensive with POEM compared to LHM ($P < 0.01$). This was mainly accounted by OR charge categories that were functions of time to complete both procedures app-eared to be the primary driver of this difference. For instance, OR labor costs, measured by activity-based costing, was $544 more expensive per case in the LHM group ($P < 0.01$ compared to POEM). Anesthesia costs, also

Table 3 Comparison of costs

Cost category	Total direct cost variance (LHM - POEM)	Average total direct cost variance	*P* value
Total direct cost variance of index admission	$27417	$1827.81	< 0.01
Anesthesia	$1322 ± 14	$88.10	0.05
EKG/telemetry	$5 ± 5	$0.3 ± 8	0.08
Laboratory	$1047 ± 32	$70 ± 116	0.05
Medical surgical supplies	$8297 ± 848	$553 ± 649	0.07
Pre-operative costs	$67 ± 17	$5 ± 13	0.84
OR services	$8169 ± 326	$545 ± 404	< 0.01
Time spent in ICU/observation	$2781 ± 303	$185 ± 509	< 0.01
Ancillary services	$166 ± 12	$11 ± 22	0.18
Cardiac services	$107 ± 4	$7 ± 10	0.13
Specialty diagnostic services	$25 ± 0.3	$2 ± 0.3	0.12
PACU costs	$70 ± 78	$46 ± 49	0.74
Pharmacy and IV therapy	$1860 ± 33	$124 ± 130	< 0.01
Physical therapy	$223 ± 13	$15 ± 1	< 0.01
Respiratory	$71 ± 71	$5 ± 65	0.76
Routine accommodations	$4377 ± 431	$292 ± 461	0.75
X-Ray	$1.117 ± 37	$75 ± 66	< 0.01
1 yr prior to index procedure	$7777	$513	0.34
1 yr after index procedure	$19730	$1315	0.68

Costs are rounded to the nearest dollar value whenever possible. POEM: Peroral endoscopic myotomy; LHM: Laparoscopic Heller myotomy; EKG: Electrocardiographic; OR: Operating room; ICU: Intensive care unit; PACU: Postanesthesia care unit.

measured by activity-based costing, were $88.10 higher ($P$ = 0.05 compared to POEM). The units for each of these charge categories were functions of time, measured by incremental 15 min time blocks required to complete the procedure. Addi -tionally, the procedure time was longer for LHM compared to POEM, thus requiring increased amount of variable cost resources such as labor utilization. Paradoxically, Miller *et al*[15] found the cost per minute for POEM procedures to be higher than LHM, further highlighting the variance in institutional charge/cost burden for these procedures. Additional charge categories that were higher in the LHM group included ICU costs, pharmacy costs, and laboratory costs, likely directly related to length of stay, which was significantly longer in the LHM group.

Our study reinforces the existing findings in terms of clinical effectiveness between POEM and LHM in the first year of follow up. Despite similar complication rates, patients undergoing LHM had accrued almost $20000 more total costs than those undergoing POEM in the year following the index procedure. Some of these costs related to prolonged hospital stays for management of complications, especially intensive care requirements in the LHM group.

The strength of our study lies in the detailed cost analysis performed, including assessment of time based OR and anesthesia costs, in addition to standard clinical outcomes and length of stay, in comparing cost-effectiveness between LHM and POEM. However, our study suffers from limitations that are inherent to retrospective studies. The procedures were performed based on the best clinical judgement, and individual patient characteristics could have impacted some of the clinical outcomes and cost metrics compared, thus introducing selection bias. Despite the patients having similar severity of achalasia symptoms, we are unsure if the patients with more severe medical complications were encouraged to have LHM *vs* POEM. However, we would suspect that the patients with more severe comorbidities would be advised to undergo less invasive endoscopic intervention, which could increase the cost associated with POEM. There was no matching between groups. It was coincidence that fifteen patients underwent POEM and fifteen underwent LHM in each group during the study time frame. Another limitation is that work-up and follow up performed outside of our institution may not have been uniformly captured. We did not have enough patients to compare cost differences between individual achalasia subtypes, as the longer myotomy needed for type 3 achalasia and esophageal body spastic disorders could generate longer procedure times for POEM, for instance. Additional research conducted across different institutions is essential to ascertain the applicability and broader relevance of our findings, considering the potential disparities in cost-charge ratios and charge valuations inherent to diverse institutions. Moreover, it is prudent to underscore the need for further studies, particularly those encompassing larger sample sizes and extended follow-up time frames. These studies would enable a comprehensive assessment of the lasting viability of our results, while also delving into the

potential variations in costs that emerge over the long term, especially concerning the heightened prevalence of gastric reflux among patients undergoing POEM.

CONCLUSION

In conclusion, we demonstrate similar effectiveness but lower costs for POEM *vs* LHM for the management of achalasia. The difference is primarily related to shorter time increments utilized in the OR during the index procedure, and shorter length of hospital stay following POEM. As POEM becomes more commonly performed in endoscopy suites *vs* OR, we speculate that costs will continue to decline. Further prospective studies are needed to determine whether POEM should be offered preferentially over LHM in the management of achalasia. Despite similar clinical outcomes, the cost of the index procedure admission for POEM was significantly lower than for LHM.

ARTICLE HIGHLIGHTS

Research background

Laparoscopic Heller myotomy (LHM) and peroral endoscopic myotomy (POEM) are two effective procedures for treating achalasia. Given the rising healthcare costs and their impact on patients and society, comparing their cost-effectiveness becomes crucial in determining the preferred management option. This research contrasts the initial procedure and short-term (1-year) costs of both techniques at a tertiary academic care center.

Research motivation

This study focuses on comparing the clinical outcomes and costs of LHM and POEM as treatments for achalasia. The key issue addressed is the lack of direct cost-effectiveness comparisons between these procedures despite their similar clinical efficacy. By demonstrating that POEM is not only clinically effective but also economically favorable due to shorter procedure times and hospital stays, this research contributes valuable insights for guiding future decisions in the management of achalasia, highlighting the importance of considering both clinical outcomes and cost factors in selecting treatment options.

Research objectives

This study's primary aim was to compare clinical outcomes and costs between LHM and POEM for achalasia. The achieved objectives include demonstrating equivalent clinical efficacy and revealing cost advantages associated with POEM, attributed to shorter procedure times and hospital stays. These realized goals provide crucial insights for future research, emphasizing the need to consider both clinical effectiveness and economic implications when making treatment decisions for achalasia.

Research methods

The study employed a retrospective chart review method to achieve its objectives. Patient data from electronic medical records were analyzed to compare clinical outcomes and costs of LHM and POEM for achalasia. Novel aspects of the research methods included a detailed cost analysis that incorporated time-based operating room (OR) and anesthesia costs, along with a comprehensive examination of various cost categories. This approach provides a unique perspective on cost-effectiveness, highlighting the potential impact of shorter procedure times and hospital stays on overall costs.

Research results

The research findings underscored the comparable clinical efficacy of LHM and POEM for achalasia treatment, as evidenced by similar post-procedure Eckardt scores. Importantly, the study revealed a significant cost advantage of POEM over LHM, primarily attributed to shorter procedure times and hospital stays. This cost-effectiveness insight provides a valuable contribution to the field, highlighting the need for a holistic approach to treatment decisions. While the study addressed the immediate costs associated with the procedures, future research should delve into long-term cost patterns and their implications.

Research conclusions

The innovative aspect lies in its detailed cost analysis, incorporating time-based OR and anesthesia costs, and its emphasis on considering both clinical effectiveness and economic implications when making treatment decisions. While not introducing new methods, the study's novelty comes from its comprehensive examination of cost categories and the recognition of the significance of shorter procedure times and hospital stays in influencing cost-effectiveness.

Research perspectives

The direction of future research in this field should encompass larger prospective studies with extended follow-up periods to validate the long-term cost-effectiveness and clinical outcomes of LHM and POEM procedures for achalasia. Additionally, investigating the evolving costs as POEM becomes more commonplace in endoscopy suites, as well as exploring variations in costs associated with individual achalasia subtypes, could provide valuable insights for informed

treatment decisions.

ACKNOWLEDGEMENTS

We thank Christopher Gerhardstein and Yucong Sang of the University of Kentucky HealthCare Finance Office for their contributions in allocating financial data for this work.

FOOTNOTES

Author contributions: Haider SA conducted primary data collection, performed data analysis, and took the lead in drafting the initial manuscript; Gyawali CP, Miller J, Softic S, and Wagh MS provided support in drafting the manuscript; Bills GS and Laoveeravat P participated in data collection, and also contributed to the study design; Gabr M played a role in shaping the overall study design, aiding in data collection, drafting the manuscript, and providing project leadership.

Institutional review board statement: The study protocol and data analysis described was approved by the University of Kentucky Institutional Review Board.

Informed consent statement: Given the retrospective nature of our study, informed consent was waived in concordance with University of Kentucky's Institutional Review Board.

Conflict-of-interest statement: All the authors report no relevant conflicts of interest for this article.

Data sharing statement: Technical appendix, statistical code, and dataset related to the manuscript titled "Comparative Analysis of Laparoscopic Heller Myotomy and Per-oral Endoscopic Myotomy for Achalasia Treatment" are available from the corresponding author at rha275@uky.edu. Informed consent was waived by the Institutional Review Board, and the presented data have been anonymized to minimize the risk of identification. The potential benefits of sharing these data outweigh the potential harms as the data contribute to scientific understanding and informed decision-making in the field of gastroenterology.

STROBE statement: The authors have read the STROBE Statement-checklist of items, and the manuscript was prepared and revised according to the STROBE Statement-checklist of items.

Country/Territory of origin: United States

ORCID number: Syedreza Ali Haider 0000-0001-7909-8597; Mihir S Wagh 0000-0003-2145-272X; Moamen Gabr 0000-0002-0069-5047.

S-Editor: Wang JJ
L-Editor: A
P-Editor: Wang JJ

REFERENCES

1 **Inoue H**, Shiwaku H, Iwakiri K, Onimaru M, Kobayashi Y, Minami H, Sato H, Kitano S, Iwakiri R, Omura N, Murakami K, Fukami N, Fujimoto K, Tajiri H. Clinical practice guidelines for peroral endoscopic myotomy. *Dig Endosc* 2018; **30**: 563-579 [PMID: 30022514 DOI: 10.1111/den.13239]

2 **Li H**, Peng W, Huang S, Ren Y, Peng Y, Li Q, Wu J, Fu X, Tang X. The 2 years' long-term efficacy and safety of peroral endoscopic myotomy for the treatment of achalasia: a systematic review. *J Cardiothorac Surg* 2019; **14**: 1 [PMID: 30606216 DOI: 10.1186/s13019-018-0811-9]

3 **Shea GE**, Johnson MK, Venkatesh M, Jolles SA, Prout TM, Shada AL, Greenberg JA, Lidor AO, Funk LM. Long-term dysphagia resolution following POEM versus Heller myotomy for achalasia patients. *Surg Endosc* 2020; **34**: 1704-1711 [PMID: 31292743 DOI: 10.1007/s00464-019-06948-y]

4 **Kumbhari V**, Tieu AH, Onimaru M, El Zein MH, Teitelbaum EN, Ujiki MB, Gitelis ME, Modayil RJ, Hungness ES, Stavropoulos SN, Shiwaku H, Kunda R, Chiu P, Saxena P, Messallam AA, Inoue H, Khashab MA. Peroral endoscopic myotomy (POEM) vs laparoscopic Heller myotomy (LHM) for the treatment of Type III achalasia in 75 patients: a multicenter comparative study. *Endosc Int Open* 2015; **3**: E195-E201 [PMID: 26171430 DOI: 10.1055/s-0034-1391668]

5 **Peng L**, Tian S, Du C, Yuan Z, Guo M, Lu L. Outcome of Peroral Endoscopic Myotomy (POEM) for Treating Achalasia Compared With Laparoscopic Heller Myotomy (LHM). *Surg Laparosc Endosc Percutan Tech* 2017; **27**: 60-64 [PMID: 28145968 DOI: 10.1097/SLE.0000000000000368]

6 **Greenleaf EK**, Winder JS, Hollenbeak CS, Haluck RS, Mathew A, Pauli EM. Cost-effectiveness of per oral endoscopic myotomy relative to laparoscopic Heller myotomy for the treatment of achalasia. *Surg Endosc* 2018; **32**: 39-45 [PMID: 29218664 DOI:

10.1007/s00464-017-5629-3]

7 **Vaezi MF**, Pandolfino JE, Yadlapati RH, Greer KB, Kavitt RT. ACG Clinical Guidelines: Diagnosis and Management of Achalasia. *Am J Gastroenterol* 2020; **115**: 1393-1411 [PMID: 32773454 DOI: 10.14309/ajg.0000000000000731]

8 **Pierre A**. Laparoscopic Heller Myotomy for Achalasia. *Oper Tech Thorac Cardiovasc Surg* 2011

9 **Inoue H**, Tianle KM, Ikeda H, Hosoya T, Onimaru M, Yoshida A, Minami H, Kudo SE. Peroral endoscopic myotomy for esophageal achalasia: technique, indication, and outcomes. *Thorac Surg Clin* 2011; **21**: 519-525 [PMID: 22040634 DOI: 10.1016/j.thorsurg.2011.08.005]

10 **American Society for Gastrointestinal Endoscopy PIVI Committee**, Chandrasekhara V, Desilets D, Falk GW, Inoue H, Romanelli JR, Savides TJ, Stavropoulos SN, Swanstrom LL. The American Society for Gastrointestinal Endoscopy PIVI (Preservation and Incorporation of Valuable Endoscopic Innovations) on peroral endoscopic myotomy. *Gastrointest Endosc* 2015; **81**: 1087-100.e1 [PMID: 25799295 DOI: 10.1016/j.gie.2014.12.007]

11 **Cotton PB**, Eisen GM, Aabakken L, Baron TH, Hutter MM, Jacobson BC, Mergener K, Nemcek A Jr, Petersen BT, Petrini JL, Pike IM, Rabeneck L, Romagnuolo J, Vargo JJ. A lexicon for endoscopic adverse events: report of an ASGE workshop. *Gastrointest Endosc* 2010; **71**: 446-454 [PMID: 20189503 DOI: 10.1016/j.gie.2009.10.027]

12 **Lee JY**, Lim CH, Kim DH, Jung HY, Youn YH, Jung DH, Park JC, Moon HS, Hong SJ; Therapeutic Endoscopy and Instrument for Functional Gastrointestinal Disorders Study Group Under the Korean Society of Neurogastroenterology and Motility. Adverse Events Associated With Peroral Endoscopic Myotomy Affecting Extended Hospital Stay: A Multi-center Retrospective Study in South Korea. *J Neurogastroenterol Motil* 2022; **28**: 247-254 [PMID: 35362451 DOI: 10.5056/jnm21081]

13 **Bhayani NH**, Kurian AA, Dunst CM, Sharata AM, Rieder E, Swanstrom LL. A comparative study on comprehensive, objective outcomes of laparoscopic Heller myotomy with per-oral endoscopic myotomy (POEM) for achalasia. *Ann Surg* 2014; **259**: 1098-1103 [PMID: 24169175 DOI: 10.1097/SLA.0000000000000268]

14 **Ujiki MB**, Yetasook AK, Zapf M, Linn JG, Carbray JM, Denham W. Peroral endoscopic myotomy: A short-term comparison with the standard laparoscopic approach. *Surgery* 2013; **154**: 893-7; discussion 897 [PMID: 24074429 DOI: 10.1016/j.surg.2013.04.042]

15 **Miller HJ**, Neupane R, Fayezizadeh M, Majumder A, Marks JM. POEM is a cost-effective procedure: cost-utility analysis of endoscopic and surgical treatment options in the management of achalasia. *Surg Endosc* 2017; **31**: 1636-1642 [PMID: 27534662 DOI: 10.1007/s00464-016-5151-z]

16 **Conte TM**, Haddad LBP, Ribeiro IB, de Moura ETH, D'Albuquerque LAC, de Moura EGH. Peroral endoscopic myotomy (POEM) is more cost-effective than laparoscopic Heller myotomy in the short term for achalasia: economic evaluation from a randomized controlled trial. *Endosc Int Open* 2020; **8**: E1673-E1680 [PMID: 33140023 DOI: 10.1055/a-1261-3417]

World Journal of Gastrointestinal Endoscopy

Submit a Manuscript: https://www.f6publishing.com

World J Gastrointest Endosc 2023 October 16; 15(10): 602-613

DOI: 10.4253/wjge.v15.i10.602

ISSN 1948-5190 (online)

ORIGINAL ARTICLE

Retrospective Cohort Study

Transoral outlet reduction: Outcomes of endoscopic Roux-en-Y gastric bypass revision in 284 patients at a community practice

Daniel B Maselli, Vibhu Chittajallu, Chase Wooley, Areebah Waseem, Daniel Lee, Michelle Secic, Lauren L Donnangelo, Brian Coan, Christopher E McGowan

Specialty type: Gastroenterology and hepatology

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification
Grade A (Excellent): 0
Grade B (Very good): B, B, B
Grade C (Good): C
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Cai KL, China; Gica N, Romania; Liao Z, Singapore; Wang ZF, China

Received: July 31, 2023
Peer-review started: July 31, 2023
First decision: August 24, 2023
Revised: August 28, 2023
Accepted: September 11, 2023
Article in press: September 11, 2023
Published online: October 16, 2023

Daniel B Maselli, Lauren L Donnangelo, Clinical Research, True You Weight Loss, Atlanta, GA 30342, United States

Vibhu Chittajallu, Department of Gastroenterology and Hepatology, University Hospitals Cleveland Medical Center, Cleveland, OH 44106, United States

Chase Wooley, Areebah Waseem, Daniel Lee, Brian Coan, Christopher E McGowan, Clinical Research, True You Weight Loss, Cary, NC 27513, United States

Michelle Secic, Secic Statistical Consulting, Cleveland, OH 44106, United States

Corresponding author: Christopher E McGowan, AGAF, FASGE, MD, Director, Clinical Research, True You Weight Loss, 2001 Weston Pkwy, Cary, NC 27513, United States. drmcgowan@trueyouweightloss.com

Abstract

BACKGROUND

Transoral outlet reduction (TORe) is a minimally invasive endoscopic revision of Roux-en-Y gastric bypass (RYGB) for weight recurrence; however, little has been published on its clinical implementation in the community setting.

AIM

To characterize the safety and efficacy of TORe in the community setting for adults with weight recurrence after RYGB.

METHODS

This is a retrospective cohort study of argon plasma coagulation and purse-string suturing for gastric outlet reduction in consecutive adults with weight recurrence after RYGB at a single community center from September 2020 to September 2022. Patients were provided longitudinal nutritional support *via* virtual visits. The primary outcome was total body weight loss (TBWL) at twelve months from TORe. Secondary outcomes included TBWL at three months and six months; excess weight loss (EWL) at three, six, and twelve months; twelve-month TBWL by obesity class; predictors of twelve-month TBWL; rates of post-TORe stenosis; and serious adverse events (SAE). Outcomes were reported with descriptive statistics.

RESULTS

Two hundred eighty-four adults (91.9% female, age 51.3 years, body mass index 39.3 kg/m^2) underwent TORe an average of 13.3 years after RYGB. Median pre- and post-TORe outlet diameter was 35 mm and 8 mm, respectively. TBWL was 11.7% ± 4.6% at three months, 14.3% ± 6.3% at six months, and 17.3% ± 7.9% at twelve months. EWL was 38.4% ± 28.2% at three months, 46.5% ± 35.4% at six months, and 53.5% ± 39.2% at twelve months. The number of follow-up visits attended was the strongest predictor of TBWL at twelve months (R^2 = 0.0139, P = 0.0005). Outlet stenosis occurred in 11 patients (3.9%) and was successfully managed with endoscopic dilation. There was one instance of post-procedural nausea requiring overnight observation (SAE rate 0.4%).

CONCLUSION

When performed by an experienced endoscopist and combined with longitudinal nutritional support, purse-string TORe is safe and effective in the community setting for adults with weight recurrence after RYGB.

Key Words: Transoral outlet reduction; Purse-string; Roux-en-Y gastric bypass; Obesity; Endoscopic revision; Weight recurrence; Gastrojejunal anastomosis

Core Tip: Given the chronic, progressive nature of obesity, weight recurrence after Roux-en-Y gastric bypass (RYGB) is common. Transoral outlet reduction (TORe) is a minimally invasive, same-day, Food and Drug Administration-authorized endoscopic procedure that restricts the gastrojejunal anastomosis to facilitate safe and clinically meaningful weight loss in patients experiencing post-RYGB weight recurrence. To date, nearly all TORe literature has originated in the academic setting. Here, we show that TORe is safe, effective, and technically feasible in the community setting when performed by an experienced bariatric endoscopist and coupled with longitudinal aftercare.

Citation: Maselli DB, Chittajallu V, Wooley C, Waseem A, Lee D, Secic M, Donnangelo LL, Coan B, McGowan CE. Transoral outlet reduction: Outcomes of endoscopic Roux-en-Y gastric bypass revision in 284 patients at a community practice. *World J Gastrointest Endosc* 2023; 15(10): 602-613

URL: https://www.wjgnet.com/1948-5190/full/v15/i10/602.htm

DOI: https://dx.doi.org/10.4253/wjge.v15.i10.602

INTRODUCTION

The Roux-en-Y gastric bypass (RYGB), characterized by its restrictive and hypoabsorptive properties, is one of the most effective therapeutic interventions for obesity. Following RYGB, patients typically reach their weight nadir between 18-24 mo, corresponding to an approximate 35% total body weight loss (TBWL). However, over the five subsequent years, there is a linear recurrence of 20%-30% of the maximal weight previously lost, thereby increasing risk for the exacerbation or recurrence of weight-associated medical conditions[1-3]. The incidence of post-RYGB weight recurrence ranges from 24%-79%, depending on patient characteristics and assessment methodology[4-6], and greater than one-third of patients will have a clinically significant weight recurrence surpassing 25% of their initial weight lost[7]. One of the strongest predictors of weight recurrence is time from RYGB, underscoring obesity's chronic, progressive nature, even after one of the most effective weight loss options currently available[8].

This natural history has led to a substantial increase in the number of revisional procedures after metabolic and bariatric surgeries—from 9480 cases in 2011 (6.0% of bariatric procedures) to 42881 cases in 2019 (16.7% of bariatric procedures)[9]. Weight recurrence after RYGB is multifactorial, and one component is dilation of the gastrojejunal anastomosis (GJA), which has been linked to a reduction in satiation from the RYGB and increased caloric intake[10]. While revisional surgery can include restriction of the gastric pouch and outlet, as well as other techniques, these interventions are associated with increased operative risk and are not widely offered after RYGB, leading to a management gap for individuals with weight recurrence[11,12].

The emergence of endobariatric therapies has provided a minimally invasive alternative for weight recurrence after metabolic and bariatric surgeries. Transoral outlet reduction (TORe) using the Apollo Revise™ System (Apollo Endosurgery, Inc., Austin, TX, United States) is now the first and only United States Food and Drug Administration (FDA)-authorized device for reduction of the GJA to induce weight loss in adults with weight recurrence after RYGB with body mass index (BMI) between 30-50 kg/m^2. TBWL after TORe ranges from 3.5%-8.6% at one year[13,14], with published durability of weight loss both after three years (TBWL 6.9% ± 10.1%) and five years (TBWL 8.8% ± 12.5%)[15].

While the principle behind TORe remains consistent—namely, reduction of the GJA—the technical approach is heterogeneous. Endoscopic suturing patterns for GJA reduction include interrupted, sequential, or purse-string suture closure, with greater efficacy at one year observed from the purse-string technique[14,15]. The GJA reduction may also take the form of argon plasma coagulation (APC) with or without full-thickness endoscopic suturing[16]. Furthermore, existing

publications of TORe nearly exclusively arise from tertiary hospital-affiliated centers, further limiting our understanding of how to successfully implement TORe in the community setting.

To address knowledge gaps surrounding the safety, efficacy, and feasibility of TORe for weight recurrence after RYGB in an ambulatory, community setting, we performed a retrospective review of prospectively collected data from 284 consecutive adults who underwent purse-string TORe with longitudinal nutritional support at a single community practice with expertise in endoscopic bariatric therapies.

MATERIALS AND METHODS

The study was approved by an Institutional Review Board (WCG IRB, Puyallup, WA) and was performed in accordance with the ethical standards of the 1964 Declaration of Helsinki. Informed consent was obtained from all individual participants included in the study. This was a retrospective study of prospectively collected data from a single community practice with expertise in endoscopic weight loss procedures. Consecutive patients aged 21 years and older undergoing TORe by a single endoscopist (Christopher E McGowan) from September 2020 to September 2022 for weight recurrence after RYGB were included. Patients were excluded from this study for the following: anti-obesity medication use within the study duration following TORe; excess weight loss (EWL) from initial RYGB < 25%; time from RYGB < 2 years; GJA diameter < 20 mm at time of TORe attempt; presence of a gastro-gastric fistula; and presence of a silastic ring at the GJA. In addition, all patients needed to describe diminished satiety from meals during their consultation to be a candidate for TORe. All subjects were self-pay. All patients underwent TORe as a same-day procedure with comprehensive virtual follow-up offered by licensed registered dieticians and scheduled visits with a medical team of physicians and nurse practitioners.

Procedural technique

All procedures were performed under general anesthesia. The steps of the TORe procedure are shown in Figure 1. First, an endoscopic evaluation with a single-channel gastroscope was performed to identify anatomy, including the gastric pouch, GJA, and blind and efferent limbs of the jejunum. TORe diameter was estimated by standard foreign body forceps, as implemented in guidelines and studies of TORe[17,18]. If present, visible surgical material was removed from the GJA with forceps and/or endoscopic scissors. If no contraindications to TORe were identified, gastric tissue surrounding the GJA was circumferentially ablated using APC (80 W, 1.2 L/min^2) for a golden-brown effect approximately 5-10 mm in width. A dual-channel therapeutic gastroscope equipped with a full thickness endoscopic suturing system (Apollo Endosurgery, Inc., Austin, TX, United States) was then used to perform a purse-string outlet reduction as described previously[14]. Outlet reduction was performed with suture tightening over a through-the-scope fluid-filled balloon inserted through the GJA and into the efferent limb for a consistent final outlet diameter. For gastric pouches > 2 cm in length, full-thickness suturing of the gastric pouch from the anterior to posterior direction was performed to reinforce the outlet and reduce the size of the pouch. All reinforcement sutures were placed within the pouch distal to the level of gastroesophageal junction.

Outcomes

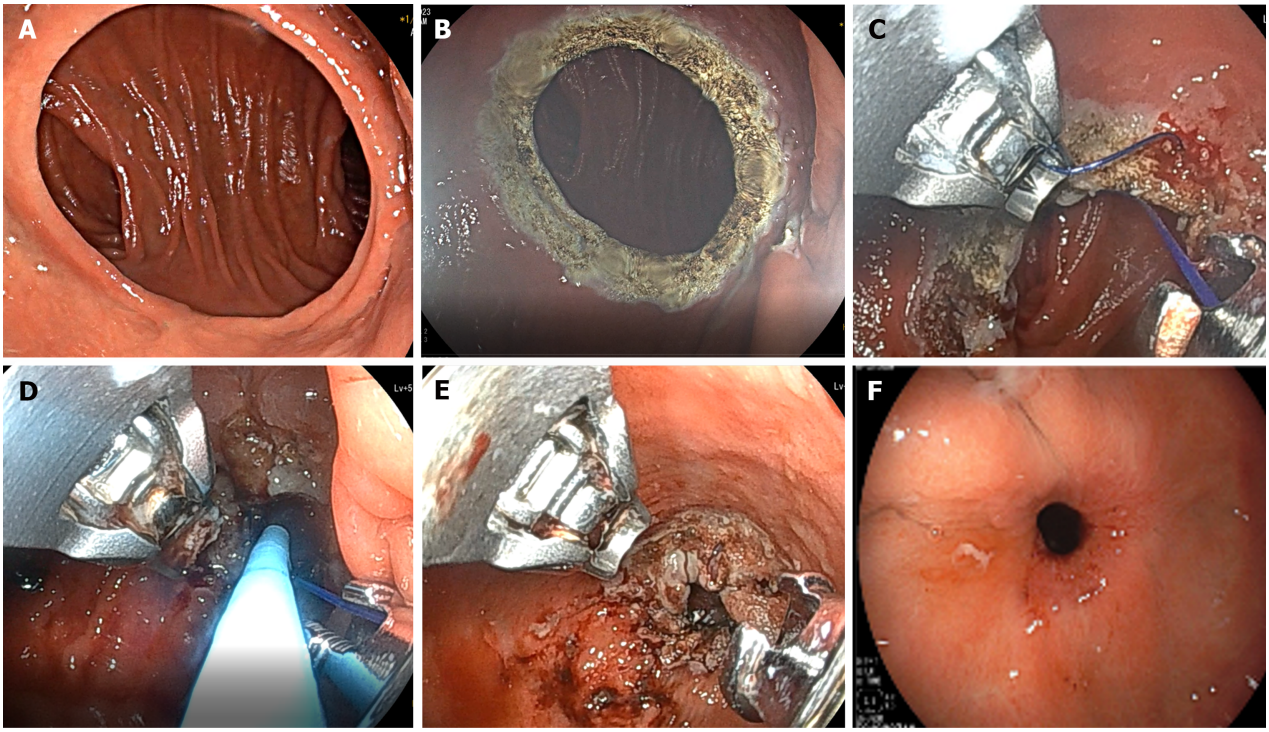
The primary outcome was TBWL at twelve months from TORe. Post-TORe TBWL was expressed as a percentage and was defined as follows: (weight at time point after TORe – weight at TORe)/ (weight at TORe) × 100. Thus, weight loss from original RYGB is not incorporated into post-TORe TBWL. Secondary outcomes included technical success; TBWL at three months and six months from TORe; TBWL at 12 mo from TORe by obesity classification; clinical response rates at 12 mo by TBWL category; EWL and body mass index (BMI) at three months, six months, and twelve months from TORe; and predictive factors of 12-mo TBWL after TORe that included age, sex, BMI, time from RYGB to TORe, percent weight recurrence from RYGB at time of TORe, procedure duration, number of sutures, post-TORe GJA diameter, and number of follow-up visits attended. Technical success was defined as the ability to perform circumferential ablation and purse-string suture pattern (*i.e.* not resorting to interrupted or running suture patterns). Weight recurrence was expressed as a percentage of weight lost from RYGB and was calculated as (weight at time of TORe – lowest weight after RYGB)/ (weight at time of RYGB – lowest weight after RYGB) × 100. At 12 mo from TORe, TBWL < 5% was considered non-response; < 10% was considered suboptimal response; ≥ 10% was considered clinically meaningful; and ≥ 15% was considered optimal response. Follow-up visits included those with either a registered dietician or medical team provider (physician or nurse practitioner). Serious adverse events were reported throughout the study and graded according to the lexicon[19]. Rates and resolution of post-TORe outlet stenosis were also reported.

Outlet stenosis and dilation

For patients who experienced post-TORe outlet stenosis, endoscopic dilations of the GJA were performed using a single-channel gastroscope and a through-the-scope fluid-filled balloon to dilate the GJA, with the goal of dilation to 2 mm beyond the initial post-TORe outlet diameter.

Statistical analysis

A biomedical statistician performed the statistical analysis of this study. One-way ANOVA was used to evaluate differences in TBWL at 12 mo between obesity classes. The remaining study data were summarized with descriptive statistics. Continuous variables were summarized with means, standard deviations, medians, and ranges. Categorical variables were summarized with counts and percentages. Multiple linear regression was performed at the 12-mo visit to



DOI: 10.4253/wjge.v15.i10.602

Figure 1 Steps of transoral outlet reduction. A: Examination of the pouch, outlet, and jejunal limbs. Gastrojejunal anastomosis (GJA) appears dilated; B: Circumferential mucosal ablation with argon plasma coagulation of the gastric tissue of GJA; C: Purse-string suturing of the outlet using the Overstitch endoscopic suturing system; D: Cinching of the suture over a through-the-scope fluid-filled balloon positioned through the outlet into the efferent jejunal limb; E: Final view of GJA after transoral outlet reduction; F: Healed appearance of GJA 12 wk after transoral outlet reduction.

evaluate predictors of TBWL and included dependent variables of age, sex, BMI, time from original RYGB, percent weight recurrence, GJA diameter, or number of sutures used.

RESULTS

Patient and procedural characteristics

Patient characteristics are shown in Table 1. This study included 284 consecutive adult patients (91.9% female, mean age 51.3 years, mean BMI 39.3 kg/m^2) who underwent TORe from September 2020 to September 2022 for weight recurrence after RYGB, without use of anti-obesity medications in the 12 mo following TORe. At the time of TORe, eight subjects (2.8%) had pre-obesity (BMI 25.0-29.9 kg/m^2), 74 (26.1%) had class I obesity (BMI 30.0-34.9 kg/m^2), 90 (31.7%) had class II obesity (BMI 35.0-39.9 kg/m^2), and 112 (39.4%) had class III obesity (BMI ≥ 40.0 kg/m^2). 159 (56.0%) patients had at least one of the following comorbidities: hypertension, hyperlipidemia, type II diabetes, or obstructive sleep apnea. From time of RYGB to post-RYGB weight nadir, the cohort had experienced TBWL of 40.5% ± 10.0%. From post-RYGB weight nadir to time of TORe, the cohort had experienced weight recurrence of 35.4% (range 5.3%-128.0%). TORe was performed an average of 13.3 years from their RYGB, took a mean of 27.5 ± 5.8 min to perform, and involved outlet reinforcement/pouch reduction sutures in 67.2% of the cases. Technical success for purse-string outlet reduction was 100%. The median pre-TORe GJA diameter was 35 mm (range 20-50 mm), and the median post-TORe GJA diameter was 8 mm (range 5-10 mm). Procedural characteristics are summarized in Table 2.

Follow-up and subject accountability

Of the 284 patients in the patient cohort at the time of data evaluation, 234, 187, and 110 were eligible for follow-up at three, six, and twelve months, respectively. Of patients eligible for follow-up, follow-up rates were 84.2%, 79.7%, and 77.3% at three, six, and twelve months, respectively. For those with 12 mo of follow-up, patients attended a median of 8 follow-up visits after TORe (range 1-17 visits).

Efficacy

TBWL following TORe was 11.7% ± 4.6% at three months, 14.3% ± 6.3% at six months, and 17.3% ± 7.9% at twelve months (Figure 2). Clinical response rates for the overall cohort are shown in Figure 3. Weight loss was similar between obesity classes at twelve months, with mean TBWL of 12.6% ± 4.3% for pre-obesity; 17.4% ± 7.8% for class I obesity; 16.4% ± 8.4% for class II obesity; and 17.3% ± 8.0% for class III obesity (P = 0.36). TBWL was 18.2% ± 7.2% for those with BMI exceeding 50 kg/m^2 (n = 11). For the overall cohort, EWL was 38.4% ± 28.2% at three months, 46.5% ± 35.4% at six months, and

Table 1 Patient characteristics

Patient Characteristics	Value
Weight at time of RYGB (kg)	
mean ± SD	134.2 ± 26.0
Median, range	130.0, 72.7-231.8
Post-RYGB weight nadir (kg)	
mean ± SD	79.0 ± 16.3
Median, range	75.0, 51.8-147.7
Weight recurrence from post-RYGB nadir to TORe (%)	
mean ± SD	39.5 ± 19.8
Median, range	35.4, 5.3-128
Duration from RYGB to TORe (yr)	13.3 ± 5.8
Weight at time of TORe (kg)	
mean ± SD	109.1 ± 20.7
Median, range	106.8, 72.7-171.4
BMI at time of TORe (kg/m^2)	
mean ± SD	39.3 ± 6.7
Median, range	38.3, 26.5-60.0
Class of obesity at time of TORe, *n* (%)	
Pre-obesity (BMI 25.1-29.9 kg/m^2)	8 (2.8)
Class I (BMI 30.0-34.9 kg/m^2)	74 (26.1)
Class II (BMI 35.0-39.9 kg/m^2)	90 (31.7)
Class III (BMI ≥ 40.0 kg/m^2)	112 (39.4%)
No. of female subjects (%)	260 (91.9)
Age at time of TORe (yr)	
mean ± SD	51.3 ± 7.9
Median, range	51, 32-72
Obesity-associated medical problems at time of TORe, *n* (%)	
Hypertension	90 (31.7%)
Dyslipidemia	74 (26.1%)
Diabetes, type II	31 (10.9%)
Obstructive sleep apnea	18 (6.3%)

Data are represented as mean ± SD and/or median, range. RYGB: Roux-en-Y gastric bypass; TORe: Transoral outlet reduction; BMI: Body mass index.

53.5% ± 39.2% at twelve months. For the overall cohort, BMI was 39.3 ± 6.6 kg/m^2 at baseline, 35.0 ± 6.4 kg/m^2 at 3 mo, 34.6 ± 7.0 kg/m^2 at 6 mo, and 33.9 ± 6.9 kg/m^2 at 12 mo. The number of follow-up visits attended was the strongest predictor of TBWL at 12 mo (R^2 = 0.139, P = 0.0005). There was no association between TBWL at 12 mo and patient age, sex, BMI, time from original RYGB, percent weight recurrence, GJA diameter, or number of sutures used. Two patients (0.7%) underwent upper endoscopy to manage insufficient clinical response. One underwent a repeat TORe with APC + endoscopic purse-string suturing for GJA dilation, and one underwent APC alone for mild stomal dilation. The overall weight trajectory of the cohort from RYGB to 12 mo after TORe is illustrated in Figure 4.

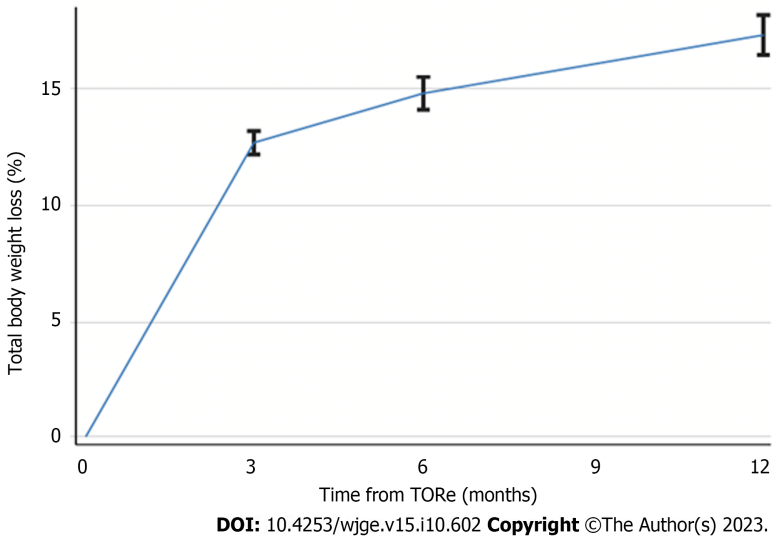
Safety

There were no instances of death, gastrointestinal bleeding, gastrointestinal tract leak or perforation, infection/sepsis, or pulmonary embolism from TORe. 283 patients (99.6%) were discharged home same-day, and one subject (0.4%) required in-patient observation for persistent vomiting, which self-resolved, representing a serious adverse event rate of 0.4%.

Table 2 Procedural characteristics of the transoral outlet reduction, *n* (%)

Procedural characteristics	Value
Procedure duration (min)	27.5 ± 12.9
Procedure Technique	
Purse-string of GJA only	93 (32.7)
Purse-string of GJA + 1 reinforcement suture in pouch	98 (34.5)
Purse-string of GJA + 2 reinforcement sutures in pouch	93 (32.7)
Pre-TORe GJA diameter estimation (mm)	
mean ± SD	33.4 ± 6.5
Median, range	35, 20-50
Post-TORe GJA diameter (mm)	
mean ± SD	7.6 ± 1.0
Median, range	8, 5-10

Data are represented as mean ± SD and/or median, range. GJA: Gastrojejunal anastomosis; TORe: Transoral outlet reduction.



DOI: 10.4253/wjge.v15.i10.602

Figure 2 Total body weight loss after transoral outlet reduction. Weight loss from time of transoral outlet reduction (TORe) is represented over the following year. Total body weight loss represents response to TORe and does not include initial weight loss to gastric bypass. TORe: transoral outlet reduction.

Outlet stenosis

Eleven patients (3.9%) developed post-TORe stenosis requiring GJA dilation. Components of outlet stenosis and management are shown in Table 3. Of the eleven patients with post-TORe stenosis, the majority (55.6%) had their GJA narrowed to 8 mm at the time of TORe. The average time from TORe to symptom onset suggestive of stenosis was 56.5 ± 30.6 d, and average time from TORe to endoscopic dilation of stenosis was 87.7 ± 60.6 d. Nine patients (81.8%) responded to a single dilation, whereas two (18.2%) required two separate endoscopic procedures for resolution. While none of these eleven patients had a history of type II diabetes, non-steroidal anti-inflammatory drug use, or tobacco use, five (45.5%) had a history of GJA stenosis following RYGB.

DISCUSSION

This study demonstrates that purse-string TORe, when performed by an experienced bariatric endoscopist and supported in conjunction with longitudinal nutritional follow-up, is safe and effective in the community setting for the management of weight recurrence after RYGB. The weight loss and safety outcomes in this cohort satisfy the expert-level thresholds for clinical adoption of a novel endoscopic bariatric therapy[20]. Over 80% of the cohort achieved > 10% TBWL, a threshold observed to have a meaningful impact on weight related medical conditions[21].

Table 3 Clinical features of stenosis of the gastrojejunal anastomosis after transoral outlet reduction, *n* (%)

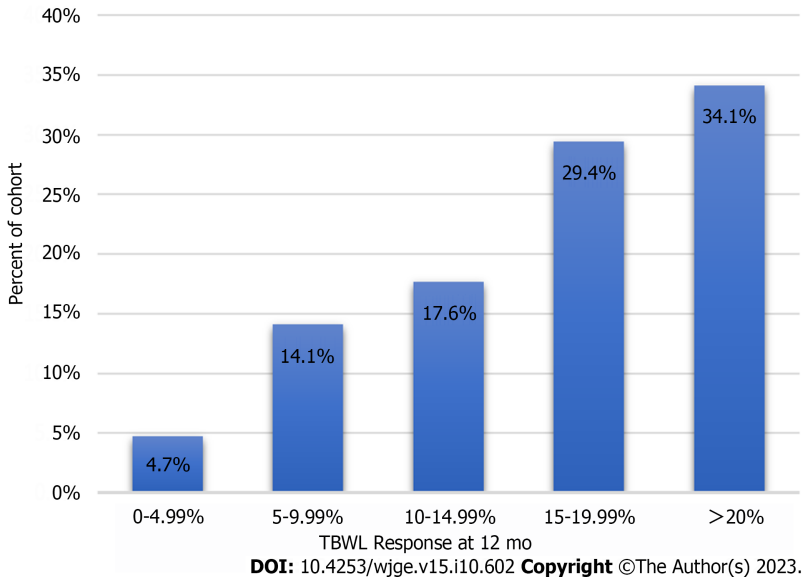
No. of patients with stenosis	11 (3.9)
Post-TORe GJA diameter (mm)	
5	1 (0.35)
6	57 (20)
7	39 (13.7)
8	158 (55.6)
9-10	25 (7.4)
Not reported	4 (1.4)
Post-Stenosis dilation diameter for resolution (mm)	
10	6 (54.5)
11	1 (9.1)
12	2 (18.2)
13.5	1 (9.1)
15	1 (9.1)
Days from TORe to symptoms suggestive of stenosis	56.5 ± 30.6
Days from TORe to first endoscopic dilation for stenosis	87.7 ± 60.6
No. of endoscopic dilations to resolve stenosis	
1	9 (82)
2	2 (18)
Medical history of patients who developed stenosis	
Post-RYGB Stenosis	5 (45.5)
Diabetes, Type II	0
NSAID Use	0
Tobacco use	0

All data is present for the eleven patients who developed gastrojejunal anastomosis stenosis after transoral outlet reduction (TORe), except for days from TORe to symptoms suggestive of stenosis, which were available for ten patients. Data represented as mean ± SD, where appropriate. GJA: gastrojejunal anastomosis; RYGB: Roux-en-Y gastric bypass; NSAID: Non-steroidal anti-inflammatory drug; TORe: Transoral outlet reduction.

Notably, TORe appears safe and effective for a wide range of BMIs, including those above or below the FDA authorized ranges of 30-50 kg/m^2. While further study is needed, we believe this shows TORe is a reasonable, minimally-invasive option for patients with BMI exceeding 50 kg/m^2, particularly given the risks of revisional surgery[12]. Additionally, obesity is a chronic, progressive disease, and increased weight recurrence attenuates the success of a revisional surgery and heightens the risk of weight-related medical conditions[22,23]. Therefore, our practice is to implement TORe for patients with weight recurrence after RYGB early, even for those with pre-obesity on a case-by-case basis, as was done here for eight subjects.

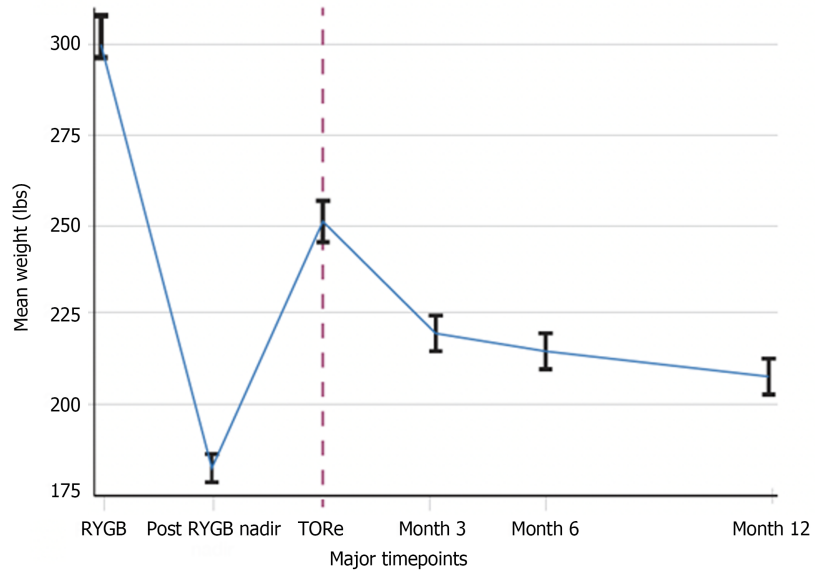
While our cohort's rates and severity of weight recurrence comport with the existing literature[2,7], a 12-mo TBWL of 17% from TORe is discordant with the published TORe experience[14,15,24]. In a systematic review and meta-analysis of thirteen studies and 850 patients, Dhindsa *et al*[25] noted a mean TBWL of 8.55% at 12 mo from TORe. While these studies also employed the same full-thickness suturing device and were predominantly female participants, major differences included the inclusion of only studies conducted at academic centers in both the inpatient and outpatient setting, inconsistent use of purse-string technique and ablation, and inclusion of patients on concomitant anti-obesity medications.

We suspect that this discrepancy is driven by two important factors within our cohort: first, consistent use of the purse-string technique, which leads to superior weight loss outcomes compared to other suture patterns for TORe[14]; second, longitudinal and frequent follow-up with medical and nutritional support, which is a critical factor in weight loss and weight loss maintenance in endobariatric therapies[26,27]. In this cohort, attendance of follow-up visits was the strongest predictor of weight loss from TORe, a feature largely afforded by a dedicated team of registered dieticians and the transition to a telemedicine care model amid the coronavirus-19 pandemic. Regular outpatient follow-up with reinforcement of comprehensive lifestyle programming likely maximizes the therapeutic effect of the TORe procedure. Finally, this may also be a result of a self-pay model in our practice, which may confer a higher degree of patient



DOI: 10.4253/wjge.v15.i10.602 **Copyright** ©The Author(s) 2023.

Figure 3 Clinical response rates at 12 mo from transoral outlet reduction. The percentage of the cohort achieving a total body weight loss response category at 12 mo is shown. Total body weight loss represents response to transoral outlet reduction and does not include initial weight loss to gastric bypass. TBWL: Total body weight loss.



DOI: 10.4253/wjge.v15.i10.602 **Copyright** ©The Author(s) 2023.

Figure 4 Weight trajectory of cohort. The mean and standard errors for weight at Roux-en-Y gastric bypass (RYGB), post-RYGB weight nadir, transoral outlet reduction (TORe), and the year after TORe are depicted for the cohort. Time for post-RYGB weight nadir is not known or specified. This figure illustrates the importance of TORe to interrupt and reverse the post-RYGB weight recurrence trajectory. RYGB: Roux-en-Y gastric bypass; TORe: Transoral outlet reduction.

investment in weight loss efforts.

As such, we recommend that gastroenterologists or surgeons looking to incorporate TORe into their practice perform the purse-string technique and provide longitudinal aftercare. The purse-string technique is more challenging to master than alternative techniques[28]. While published data on the learning curve for TORe are sparse, our experience mirrors that of the endoscopic sleeve gastroplasty, for which 25-50 cases are needed, at minimum[29]. However, a novel endoscopic suturing simulator has shown promise in markedly reducing the number of cases needed for independence in TORe, including among novices[30].

Intriguingly, pouch reduction did not contribute to a greater weight loss at one year. This is suggestive of a few possibilities: first, narrowing of the GJA disproportionately governs satiation signals compared to pouch restriction, and second, mucosal ablation and purse-string suturing of the GJA may lead to a durable construct that is not enhanced within the first year by additional reinforcement sutures. Mucosal ablation of the pouch in combination with endoscopic suturing was not performed in this study, and the effect of this is not known at this time. Other factors previously shown to be associated with greater weight loss after TORe—including degree of weight recurrence following RYGB, smaller GJA

post-TORe, greater change in pre- to post-TORe diameter, and number of pouch sutures— were not noted in our study [16,31,32].

For those wishing to provide or undergo this procedure, it is important to be cognizant of post-TORe stenosis. This presents as a consistent inability to pass ingested meals with subsequent regurgitation and is not responsive to prolonging a liquid diet. From our cohort, post-TORe stenosis followed a predictable timeline, predominantly occurring within a few weeks of starting a regular diet (day 50 in our program). The major risk factor appears to be GJA stenosis after RYGB; thus, it is routine to ask about this during consultation for TORe at our center. In these patients, our approach is modified by narrowing the GJA to 10 mm rather than 8 mm, our current standard practice. The rate of post-TORe stenosis observed in this cohort is consistent with those published by Jaruvongvanich *et al*[16] but nearly ten times higher than those observed in Jirapinyo *et al*[31] and Dhindsa *et al*[25]. We suspect that this is driven by the high wattage (80 W) mucosal ablation—which is associated with a higher absolute rate of stenosis—plus the purse-string suture technique [33]. The combination of these approaches may be more likely to induce an overly robust healing response beyond the original post-TORe diameter in a predisposed patient. Nevertheless, given that this combination technique offers superior weight loss outcomes, we contend this is an acceptable risk, provided patients are sufficiently counseled and aware that it typically resolves with one to two endoscopic dilations.

Adverse event rates in our cohort were otherwise lower than other published studies, with only one patient admitted for overnight observation of persistent nausea and vomiting with self-resolution[25]. Still, as with other endoscopic suturing procedures, TORe can be associated with a low but serious risk of gastrointestinal bleeding, intraabdominal infection, perigastric leak, and perforation[25,34]. It is therefore critical to inform patients about warning signs and symptoms and to ensure that they have direct access to an on-call physician for assessment and risk stratification should concerns arise. Though this study showed that TORe can be successfully and safely performed in a community ambulatory surgical center, these rare complications may require inpatient management. As such, community physicians performing TORe should have privileges at or at least a relationship with nearby hospitals.

Strengths of this study include a consistent TORe procedural technique and a high subject accountability rate over twelve months. Study limitations include its single-center, retrospective design, and procedural performance by a single experienced endoscopist with expertise in endobariatric procedures, as these limit the generalizability of our findings. Restricting the study duration to 12 mo was necessary due to loss of follow-up beyond this time point but precludes understanding of TORe durability beyond one year. Other limitations include lack of follow-up on comorbidity resolution and lack of capture of improvement of dumping syndrome, for which TORe is a proposed therapy[34,35]. Finally, the results here are, by definition, from those patients who continued with follow-up, and—given that follow-up support is linked to improved weight loss outcomes in endobariatrics—this cohort may over-represent weight loss response[26,27]. For this reason, we emphasize the importance of both TORe technique and aftercare in the interpretation of these data.

Ultimately, TORe provides a critically needed tool for addressing weight recurrence after metabolic and bariatric surgery for those wishing to avoid the risks of revisional surgery. While there are still challenges, including accessibility due to the lack of widespread insurance coverage in the United States and inconsistency regarding what constitutes sufficient training to obtain competency in TORe[36], the procedure nevertheless fits well within the model of obesity as a chronic, progressive, relapsing disease state, particularly as it has been shown to be safe to use with anti-obesity pharmacotherapy[15,37] and, as seen with two patients in our cohort, can be repeated to enhance weight loss effect.

CONCLUSION

When performed by a physician with experience in endoscopic bariatric therapies, TORe is a feasible, safe, and effective approach to weight recurrence after RYGB in a community-based practice. Successful TORe implementation should focus on mucosal ablation with purse-string technique and frequent, intensive aftercare. Patients and providers should be aware of the risk of post-TORe stenosis that responds well to non-urgent endoscopic balloon dilation.

ARTICLE HIGHLIGHTS

Research background

Given the chronic, progressive nature of obesity, recurrence of 20%-30% of weight lost is common in the decade following Roux-en-Y gastric bypass (RYGB).

Research motivation

Surgical interventions for weight recurrence after RYGB carry heightened risks. Patients may be more amenable to the minimally-invasive endoscopic revision known as transoral outlet reduction (TORe). Though United States Food and Drug Administration-authorized, very little data exists on the implementation of TORe in the community setting.

Research objectives

To clarify the safety, efficacy, and technically feasibility of purse-string TORe in the community setting.

Research methods

This was a retrospective evaluation of a prospectively-maintained cohort of adult patients undergoing purse-string TORe in an ambulatory surgical center at a practice with expertise in endoscopic bariatric therapies. The primary outcome was total body weight loss at 12 mo. Secondary outcomes included excess weight loss within the first year, safety, predictors of total body weight loss (TBWL) response at 12 mo, and rates of post-TORe gastrojejunal anastomosis (GJA) stenosis.

Research results

In this cohort of 284 adults who underwent TORe in the community setting for weight recurrence following RYGB, 12-mo total body weight loss was 17.4%, and 81.2% achieved ≥ 10% TBWL. The number of follow up visits was the strongest predictor of 12-mo TBWL. Serious adverse events were rare and included one episode of post-operative nausea and vomiting requiring hospitalization (0.4%). Post-TORe stenosis occurred in 3.9% of subjects after an average of 57 d from TORe and was successfully managed with 1-2 endoscopic dilations. In this single largest cohort of patients undergoing TORe with a consistent purse-string technique, the procedure was shown to be safe and effective in the community setting.

Research conclusions

When performed by experienced endoscopists and supported by longitudinal nutritional aftercare, purse-string TORe is an effective, safe, and feasible tool in the community setting to address weight recurrence after RYGB.

Research perspectives

Further study of TORe should evaluate the impact of the procedure on weight related comorbidities, which are shown to reemerge with weight recurrence after RYGB. Investigation into application of TORe to other metabolic and bariatric surgeries with a GJA (such as the one-anastomosis gastric bypass) and other clinical entities in RYGB (such as dumping syndrome and bile acid reflux) will also be valuable to the field.

FOOTNOTES

Author contributions: Maselli DB protocol preparation, manuscript preparation and revision; Chittajallu V manuscript preparation; Waseem A protocol preparation, manuscript revision; Lee D data collection, manuscript revision; Secic M statistical analysis; Wooley C protocol preparation, manuscript revision; Donnangelo LL manuscript revision; Coan B manuscript revision; McGowan CE study conceptualization, protocol preparation, manuscript revision.

Institutional review board statement: The study was approved by an Institutional Review Board (WCG IRB, Puyallup, WA).

Informed consent statement: All subjects provided signed consent for their data to be used for scientific publication.

Conflict-of-interest statement: Dr. Daniel B Maselli is a consultant for Apollo Endosurgery, with no proprietary relationship. Dr. Christopher E McGowan previously served as a consultant for Apollo Endosurgery from 2019-2022, with no proprietary relationship. Dr. Vibhu Chittajallu, Dr. Lauren L Donnangelo, Dr. Brian Coan, Mr. Chase Wooley, Ms. Areebah Waseem, Ms. Michelle Secic, and Mr. Daniel Lee have no conflicts of interest or financial ties to disclose.

Data sharing statement: Data can be made available from the corresponding author at drmcgowan@trueyouweightloss.com.

Country/Territory of origin: United States

ORCID number: Daniel B Maselli 0000-0002-8605-6966; Christopher E McGowan 0000-0001-8698-0932.

Corresponding Author's Membership in Professional Societies: American Gastroenterological Association; American Society for Gastrointestinal Endoscopy.

S-Editor: Li L
L-Editor: A
P-Editor: Cai YX

REFERENCES

1 **Thomas DD**, Anderson WA, Apovian CM, Hess DT, Yu L, Velazquez A, Carmine B, Istfan NW. Weight Recidivism After Roux-en-Y Gastric Bypass Surgery: An 11-Year Experience in a Multiethnic Medical Center. *Obesity (Silver Spring)* 2019; **27**: 217-225 [PMID: 30421862 DOI:

10.1002/oby.22360]
2 **Adams TD**, Davidson LE, Litwin SE, Kim J, Kolotkin RL, Nanjee MN, Gutierrez JM, Frogley SJ, Ibele AR, Brinton EA, Hopkins PN, McKinlay R, Simper SC, Hunt SC. Weight and Metabolic Outcomes 12 Years after Gastric Bypass. *N Engl J Med* 2017; **377**: 1143-1155 [PMID: 28930514 DOI: 10.1056/NEJMoa1700459]
3 **Sjöström L**, Lindroos AK, Peltonen M, Torgerson J, Bouchard C, Carlsson B, Dahlgren S, Larsson B, Narbro K, Sjöström CD, Sullivan M, Wedel H; Swedish Obese Subjects Study Scientific Group. Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. *N Engl J Med* 2004; **351**: 2683-2693 [PMID: 15616203 DOI: 10.1056/NEJMoa035622]
4 **Monaco-Ferreira DV**, Leandro-Merhi VA. Weight Regain 10 Years After Roux-en-Y Gastric Bypass. *Obes Surg* 2017; **27**: 1137-1144 [PMID: 27798793 DOI: 10.1007/s11695-016-2426-3]
5 **Magro DO**, Geloneze B, Delfini R, Pareja BC, Callejas F, Pareja JC. Long-term weight regain after gastric bypass: a 5-year prospective study. *Obes Surg* 2008; **18**: 648-651 [PMID: 18392907 DOI: 10.1007/s11695-007-9265-1]
6 **Odom J**, Zalesin KC, Washington TL, Miller WW, Hakmeh B, Zaremba DL, Altattan M, Balasubramaniam M, Gibbs DS, Krause KR, Chengelis DL, Franklin BA, McCullough PA. Behavioral predictors of weight regain after bariatric surgery. *Obes Surg* 2010; **20**: 349-356 [PMID: 19554382 DOI: 10.1007/s11695-009-9895-6]
7 **Cooper TC**, Simmons EB, Webb K, Burns JL, Kushner RF. Trends in Weight Regain Following Roux-en-Y Gastric Bypass (RYGB) Bariatric Surgery. *Obes Surg* 2015; **25**: 1474-1481 [PMID: 25595383 DOI: 10.1007/s11695-014-1560-z]
8 **Shantavasinkul PC**, Omotosho P, Corsino L, Portenier D, Torquati A. Predictors of weight regain in patients who underwent Roux-en-Y gastric bypass surgery. *Surg Obes Relat Dis* 2016; **12**: 1640-1645 [PMID: 27989521 DOI: 10.1016/j.soard.2016.08.028]
9 **Clapp B**, Ponce J, DeMaria E, Ghanem O, Hutter M, Kothari S, LaMasters T, Kurian M, English W. American Society for Metabolic and Bariatric Surgery 2020 estimate of metabolic and bariatric procedures performed in the United States. *Surg Obes Relat Dis* 2022; **18**: 1134-1140 [PMID: 35970741 DOI: 10.1016/j.soard.2022.06.284]
10 **Maleckas A**, Gudaitytė R, Petereit R, Venclauskas L, Veličkienė D. Weight regain after gastric bypass: etiology and treatment options. *Gland Surg* 2016; **5**: 617-624 [PMID: 28149808 DOI: 10.21037/gs.2016.12.02]
11 **Tran DD**, Nwokeabia ID, Purnell S, Zafar SN, Ortega G, Hughes K, Fullum TM. Revision of Roux-En-Y Gastric Bypass for Weight Regain: a Systematic Review of Techniques and Outcomes. *Obes Surg* 2016; **26**: 1627-1634 [PMID: 27138603 DOI: 10.1007/s11695-016-2201-5]
12 **Pokala B**, Giannopoulos S, Athanasiadis DI, Motamedi SMK, Stefanidis D. Distal gastric bypass revision for weight recurrence or nonresponse to primary procedure: initial experience and outcomes in an academic practice. *Surg Endosc* 2023; **37**: 5538-5546 [PMID: 36261645 DOI: 10.1007/s00464-022-09719-4]
13 **Thompson CC**, Chand B, Chen YK, DeMarco DC, Miller L, Schweitzer M, Rothstein RI, Lautz DB, Slattery J, Ryan MB, Brethauer S, Schauer P, Mitchell MC, Starpoli A, Haber GB, Catalano MF, Edmundowicz S, Fagnant AM, Kaplan LM, Roslin MS. Endoscopic suturing for transoral outlet reduction increases weight loss after Roux-en-Y gastric bypass surgery. *Gastroenterology* 2013; **145**: 129-137.e3 [PMID: 23567348 DOI: 10.1053/j.gastro.2013.04.002]
14 **Schulman AR**, Kumar N, Thompson CC. Transoral outlet reduction: a comparison of purse-string with interrupted stitch technique. *Gastrointest Endosc* 2018; **87**: 1222-1228 [PMID: 29108984 DOI: 10.1016/j.gie.2017.10.034]
15 **Jirapinyo P**, Kumar N, AlSamman MA, Thompson CC. Five-year outcomes of transoral outlet reduction for the treatment of weight regain after Roux-en-Y gastric bypass. *Gastrointest Endosc* 2020; **91**: 1067-1073 [PMID: 31816315 DOI: 10.1016/j.gie.2019.11.044]
16 **Jaruvongvanich V**, Vantanasiri K, Laoveeravat P, Matar RH, Vargas EJ, Maselli DB, Alkhatry M, Fayad L, Kumbhari V, Fittipaldi-Fernandez RJ, Hollenbach M, Watson RR, Gustavo de Quadros L, Galvao Neto M, Aepli P, Staudenmann D, Brunaldi VO, Storm AC, Martin JA, Gomez V, Abu Dayyeh BK. Endoscopic full-thickness suturing plus argon plasma mucosal coagulation versus argon plasma mucosal coagulation alone for weight regain after gastric bypass: a systematic review and meta-analysis. *Gastrointest Endosc* 2020; **92**: 1164-1175.e6 [PMID: 32692991 DOI: 10.1016/j.gie.2020.07.013]
17 **Brunaldi VO**, Peixoto de Oliveira GH, Kerbage A, Ribas PH, Nunes F, Faria G, de Moura D, Riccioppo D, Santo M, de Moura E. Long-term follow-up after transoral outlet reduction following Roux-en-Y gastric bypass: Back to stage 0? *Endosc Int Open* 2023; **11**: E538-E545 [PMID: 37251791 DOI: 10.1055/a-2075-1198]
18 **Galvao Neto M**, Brunaldi VO, Grecco E, Silva LB, de Quadros LG, de Souza TF, Teixeira A, de Morais HWP, de Lima JHF, Concon Filho A, Amorim A, de Santana MF, Teixeira N, Marchesini JC; Brazilian Bariatric Endoscopy Collaborative working group. Good Clinical Practices on Argon Plasma Coagulation Treatment for Weight Regain Associated with Dilated Gastrojejunostomy Following Roux-en-Y Gastric Bypass: a Brazilian-Modified Delphi Consensus. *Obes Surg* 2022; **32**: 273-283 [PMID: 34811645 DOI: 10.1007/s11695-021-05795-y]
19 **Cotton PB**, Eisen GM, Aabakken L, Baron TH, Hutter MM, Jacobson BC, Mergener K, Nemcek A Jr, Petersen BT, Petrini JL, Pike IM, Rabeneck L, Romagnuolo J, Vargo JJ. A lexicon for endoscopic adverse events: report of an ASGE workshop. *Gastrointest Endosc* 2010; **71**: 446-454 [PMID: 20189503 DOI: 10.1016/j.gie.2009.10.027]
20 **Abu Dayyeh BK**, Kumar N, Edmundowicz SA, Jonnalagadda S, Larsen M, Sullivan S, Thompson CC, Banerjee S; ASGE Bariatric Endoscopy Task Force and ASGE Technology Committee. ASGE Bariatric Endoscopy Task Force systematic review and meta-analysis assessing the ASGE PIVI thresholds for adopting endoscopic bariatric therapies. *Gastrointest Endosc* 2015; **82**: 425-38.e5 [PMID: 26232362 DOI: 10.1016/j.gie.2015.03.1964]
21 **Ryan DH**, Yockey SR. Weight Loss and Improvement in Comorbidity: Differences at 5%, 10%, 15%, and Over. *Curr Obes Rep* 2017; **6**: 187-194 [PMID: 28455679 DOI: 10.1007/s13679-017-0262-y]
22 **Łabul M**, Wysocki M, Bartosiak K, Orłowski M, Katkowski B, Jaworski P, Małczak P, Major P; PROSS–Collaborative Study Group. Analysis of the Factors Contributing to Bariatric Success After Laparoscopic Redo Bariatric Procedures: Results from Multicenter Polish Revision Obesity Surgery Study (PROSS). *Obes Surg* 2022; **32**: 3879-3890 [PMID: 36242680 DOI: 10.1007/s11695-022-06306-3]
23 **Bray GA**, Kim KK, Wilding JPH; World Obesity Federation. Obesity: a chronic relapsing progressive disease process. A position statement of the World Obesity Federation. *Obes Rev* 2017; **18**: 715-723 [PMID: 28489290 DOI: 10.1111/obr.12551]
24 **Vargas EJ**, Bazerbachi F, Rizk M, Rustagi T, Acosta A, Wilson EB, Wilson T, Neto MG, Zundel N, Mundi MS, Collazo-Clavell ML, Meera S, Abu-Lebdeh HS, Lorentz PA, Grothe KB, Clark MM, Kellogg TA, McKenzie TJ, Kendrick ML, Topazian MD, Gostout CJ, Abu Dayyeh BK. Transoral outlet reduction with full thickness endoscopic suturing for weight regain after gastric bypass: a large multicenter international experience and meta-analysis. *Surg Endosc* 2018; **32**: 252-259 [PMID: 28664438 DOI: 10.1007/s00464-017-5671-1]
25 **Dhindsa BS**, Saghir SM, Naga Y, Dhaliwal A, Ramai D, Cross C, Singh S, Bhat I, Adler DG. Efficacy of transoral outlet reduction in Roux-en-Y gastric bypass patients to promote weight loss: a systematic review and meta-analysis. *Endosc Int Open* 2020; **8**: E1332-E1340 [PMID:

33015335 DOI: 10.1055/a-1214-5822]

26 **Lopez-Nava G**, Galvao M, Bautista-Castaño I, Fernandez-Corbelle JP, Trell M. Endoscopic sleeve gastroplasty with 1-year follow-up: factors predictive of success. *Endosc Int Open* 2016; **4**: E222-E227 [PMID: 26878054 DOI: 10.1055/s-0041-110771]

27 **Lopez-Nava G**, Asokkumar R, Rull A, Corbelle F, Beltran L, Bautista I. Bariatric endoscopy procedure type or follow-up: What predicted success at 1 year in 962 obese patients? *Endosc Int Open* 2019; **7**: E1691-E1698 [PMID: 31803819 DOI: 10.1055/a-1007-1769]

28 **Jirapinyo P**, Thompson CC. Training in Bariatric and Metabolic Endoscopic Therapies. *Clin Endosc* 2018; **51**: 430-438 [PMID: 30301319 DOI: 10.5946/ce.2018.148]

29 **Saumoy M**, Schneider Y, Zhou XK, Shukla A, Kahaleh M, Aronne L, Sharaiha RZ. A single-operator learning curve analysis for the endoscopic sleeve gastroplasty. *Gastrointest Endosc* 2018; **87**: 442-447 [PMID: 28843586 DOI: 10.1016/j.gie.2017.08.014]

30 **Jirapinyo P**, Thompson CC. Development of a Novel Endoscopic Suturing Simulator: Validation and Impact on Clinical Learning Curve. *Gastrointest Endosc* 2023 [PMID: 37536634 DOI: 10.1016/j.gie.2023.07.045]

31 **Jirapinyo P**, Kröner PT, Thompson CC. Purse-string transoral outlet reduction (TORe) is effective at inducing weight loss and improvement in metabolic comorbidities after Roux-en-Y gastric bypass. *Endoscopy* 2018; **50**: 371-377 [PMID: 29253919 DOI: 10.1055/s-0043-122380]

32 **Meyers MH**, Swei EC, Tarter W, Schoen J, Rothchild K, Pratap A, Sullivan SA. Factors Associated with Weight Loss After Endoscopic Transoral Outlet Reduction (TORe). *J Gastrointest Surg* 2023; **27**: 1587-1593 [PMID: 37237090 DOI: 10.1007/s11605-023-05695-9]

33 **Jirapinyo P**, de Moura DTH, Dong WY, Farias G, Thompson CC. Dose response for argon plasma coagulation in the treatment of weight regain after Roux-en-Y gastric bypass. *Gastrointest Endosc* 2020; **91**: 1078-1084 [PMID: 31904378 DOI: 10.1016/j.gie.2019.12.036]

34 **Pontecorvi V**, Matteo MV, Bove V, De Siena M, Giannetti G, Carlino G, Polidori G, Vinti L, Angelini G, Iaconelli A, Familiari P, Raffaelli M, Costamagna G, Boškoski I. Long-term Outcomes of Transoral Outlet Reduction (TORe) for Dumping Syndrome and Weight Regain After Roux-en-Y Gastric Bypass. *Obes Surg* 2023; **33**: 1032-1039 [PMID: 36702981 DOI: 10.1007/s11695-023-06466-w]

35 **Vargas EJ**, Abu Dayyeh BK, Storm AC, Bazerbachi F, Matar R, Vella A, Kellogg T, Stier C. Endoscopic management of dumping syndrome after Roux-en-Y gastric bypass: a large international series and proposed management strategy. *Gastrointest Endosc* 2020; **92**: 91-96 [PMID: 32112780 DOI: 10.1016/j.gie.2020.02.029]

36 **Spota A**, Laracca GG, Perretta S. Training in bariatric and metabolic endoscopy. *Ther Adv Gastrointest Endosc* 2020; **13**: 2631774520931978 [PMID: 32596663 DOI: 10.1177/2631774520931978]

37 **Jirapinyo P**, Thompson CC. Combining transoral outlet reduction with pharmacotherapy yields similar 1-year efficacy with improved safety compared with surgical revision for weight regain after Roux-en-Y gastric bypass (with videos). *Gastrointest Endosc* 2023 [PMID: 37150416 DOI: 10.1016/j.gie.2023.04.2092]

World Journal of Gastrointestinal Endoscopy

Submit a Manuscript: https://www.f6publishing.com

World J Gastrointest Endosc 2023 October 16; 15(10): 614-622

DOI: 10.4253/wjge.v15.i10.614

ISSN 1948-5190 (online)

ORIGINAL ARTICLE

Retrospective Study

Efficacy and safety of endoscopic retrograde cholangiopancreatography in recurrent pancreatitis of pediatric asparaginase-associated pancreatitis

Kai-Hua Yang, Jing-Qing Zeng, Sheng Ding, Tian-Ao Zhang, Wen-Yu Wang, Jia-Yu Zhang, Lan Wang, Jian Xiao, Biao Gong, Zhao-Hui Deng

Specialty type: Gastroenterology and hepatology

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): 0
Grade C (Good): C
Grade D (Fair): D
Grade E (Poor): 0

P-Reviewer: Amornyotin S, Thailand; Gupta R, India

Received: June 19, 2023
Peer-review started: June 19, 2023
First decision: August 11, 2023
Revised: August 26, 2023
Accepted: September 14, 2023
Article in press: September 14, 2023
Published online: October 16, 2023

Kai-Hua Yang, Jing-Qing Zeng, Sheng Ding, Tian-Ao Zhang, Wen-Yu Wang, Jia-Yu Zhang, Lan Wang, Jian Xiao, Zhao-Hui Deng, Department of Gastroenterology, Shanghai Children's Medical Center, Shanghai Jiao Tong University School of Medicine, Shanghai 200127, China

Biao Gong, Department of Gastroenterology, Shanghai Shuguang Hospital, Shanghai University of Traditional Chinese Medicine, Shanghai 200120, China

Corresponding author: Zhao-Hui Deng, PhD, Chief Physician, Department of Gastroenterology, Shanghai Children's Medical Center, Shanghai Jiao Tong University School of Medicine, No. 1678 Dongfang Road, Shanghai 200127, China. dzhrj@163.com

Abstract

BACKGROUND

Asparaginase (ASP) is an important drug in combined chemotherapy regimens for pediatric acute lymphoblastic leukemia (ALL); ASP-associated pancreatitis (AAP) is the main adverse reaction of ASP. Recurrent pancreatitis is a complication of AAP, for which medication is ineffective.

AIM

To evaluate the efficacy and safety of endoscopic retrograde cholangiopancreatography (ERCP) in treating recurrent pancreatitis due to AAP.

METHODS

From May 2018 to August 2021, ten children (five males and five females; age range: 4–13 years) with AAP were treated using ERCP due to recurrent pancreatitis. Clinical data of the ten children were collected, including their sex, age, weight, ALL risk grading, clinical symptoms at the onset of pancreatitis, time from the first pancreatitis onset to ERCP, ERCP operation status, and postoperative complications. The symptomatic relief, weight change, and number of pancreatitis onsets before and after ERCP were compared.

RESULTS

The preoperative symptoms were abdominal pain, vomiting, inability to eat, weight loss of 2–7 kg, and 2–9 pancreatitis onsets. After the operation, nine of ten patients did not develop pancreatitis, had no abdominal pain, could eat normally;

the remaining patient developed three pancreatitis onsets due to the continuous administration of ASP, but eating was not affected. The postoperative weight gain was 1.5–8 kg. There was one case of post ERCP pancreatitis and two cases of postoperative infections; all recovered after medication.

CONCLUSION
ERCP improved clinical symptoms and reduced the incidence of pancreatitis, and was shown to be a safe and effective method for improving the management of recurrent pancreatitis due to AAP.

Key Words: Acute lymphoblastic leukemia; Asparaginase; Endoscopic retrograde cholangiopancreatography; Pancreatic pseudocyst; Recurrent pancreatitis; Children

Core Tip: Recurrent pancreatitis is a complication of asparaginase-associated pancreatitis (AAP), and medications do not prevent recurrence. This study was conducted to evaluate the efficacy and safety of endoscopic retrograde cholangiopancreatography (ERCP) in treating recurrent pancreatitis due to AAP. Our research found that ERCP improved clinical symptoms and reduced the incidence of pancreatitis, and was shown to be a safe and effective method for improving the management of recurrent pancreatitis due to AAP.

Citation: Yang KH, Zeng JQ, Ding S, Zhang TA, Wang WY, Zhang JY, Wang L, Xiao J, Gong B, Deng ZH. Efficacy and safety of endoscopic retrograde cholangiopancreatography in recurrent pancreatitis of pediatric asparaginase-associated pancreatitis. *World J Gastrointest Endosc* 2023; 15(10): 614-622
URL: https://www.wjgnet.com/1948-5190/full/v15/i10/614.htm
DOI: https://dx.doi.org/10.4253/wjge.v15.i10.614

INTRODUCTION

Acute lymphoblastic leukemia (ALL) is a malignant tumor with a high incidence in children. One of the key drugs in the combined chemotherapy regimen to treat ALL is asparaginase (ASP). ASP is important for inducing remission and achieving long-term disease-free survival, but it has a high probability of inducing ASP-associated pancreatitis (AAP). The overall incidence of AAP is 2%–18%, with 7%–66% of cases classified as severe; the mortality rate due to AAP is as high as 2%[1-5]. Asparaginase-induced pancreatitis is often seen as acute toxicity with lasting issues such as recurrent pancreatitis, causing patients to be at risk for progressing to chronic pancreatitis over time. This may affect children's eating, weight, and quality of life[6-11]. Recurrent pancreatitis is the main complication of AAP, wherein children are unable to eat normally and lose weight, thus seriously affecting their quality of life[6-11]. If pancreatitis repeatedly recurs in AAP, the effects of medications such as somatostatin and its analog octreotide are not efficacious for preventing recurrent pancreatitis, which is a difficulty in clinical treatment.

Endoscopic retrograde cholangiopancreatography (ERCP) is a minimally invasive method for diagnosing and treating recurrent pancreatitis, and its efficacy and safety have been confirmed[12-17]. As patients with ALL are special, research has seldom focused on procedures for the complication of ASP. This study aimed to evaluate the efficacy and safety of ERCP in treating recurrent pancreatitis due to AAP.

MATERIALS AND METHODS

General information

This study was approved by the Institutional Review Board of Shanghai Children's Medical Center (SCMCIRB-K2019005). All the participants' legal guardians provided written informed consent. From May 2018 to August 2021, ten children with AAP underwent ERCP due to recurrent pancreatitis that persisted for 3 mo and for which medication was ineffective. Their sex, age, ALL risk grading, clinical symptoms at the onset of pancreatitis, time from the first pancreatitis onset to ERCP, weight, ERCP operation status, and postoperative complications of ERCP were summarized. The status of symptomatic relief, number of pancreatitis onsets, and weight change before and after ERCP operation were compared. For all ten children, smoking, alcohol consumption, biliary pancreatitis, hyperlipidemia, hypercalcemia, tumor invasion, trauma, and autoimmune diseases were excluded.

Definitions

AAP was defined as acute pancreatitis after using ASP, and its diagnosis was based on a combination of clinical, biochemical (amylase, lipase), and imaging evidence. According to the diagnostic criteria put forward by the Toxicity Working Group established by the Ponte di Legno consortium in 2016, cases that meet two or more of the following

criteria can be diagnosed as having AAP[18,19]: (1) Acute pancreatitis-related abdominal pain; (2) blood amylase or blood lipase exceeding three times the upper limit of normal; and (3) imaging examination findings (ultrasonography, computed tomography, or magnetic resonance imaging) consistent with pancreatitis.

ERCP procedures

Prior to ERCP, each child's guardian signed a written informed consent for the procedure. All procedures were performed by the same experienced endoscopist, who had, incidentally, performed more than 30000 ERCPs. The children underwent ERCP in the prone position under general anesthesia using a standard pediatric duodenoscope (JF-240, Olympus, Tokyo, Japan), and vital signs were continuously monitored. Therapeutic maneuvers were selected during the operation according to the pancreatic imaging results, including endoscopic pancreatography sphincterotomy, placement of pancreatic duct stent, balloon dilation, and stone extraction. Figure 1A and B show the most common ERCP procedures of stone extraction and placement of pancreatic duct stent. The fluoroscopic view of the pancreatic duct is shown in Figure 1C. A fluoroscopic view of the pancreatic duct stricture dilation performed by balloon manipulation and huge pseudocyst is shown in Figure 1D. Post-ERCP complications were assessed by monitoring the child's blood amylase and lipase levels, using pancreatic ultrasound images, and assessing postoperative abdominal pain, fever, and bleeding 24 h after ERCP. Post-ERCP complications were treated using the conventional treatment in internal medicine, and further evaluation and treatment were required for children with severe disease. The discharge criteria were absence of fever and abdominal pain along with a return of blood amylase levels to normal. Patients who did not meet the discharge criteria were evaluated for treatment.

Follow-up and evaluation indicators

Follow-up time: All patients were followed up for an average of 1.2 years, the shortest follow-up time was 1 year and the longest was 1.5 years.

Observation indicators: The primary observation indicators, including the number of acute pancreatitis onsets, symptoms related to acute pancreatitis such as abdominal pain, vomiting, normal eating habits, and body weight were evaluated every 3 mo. Those with pancreatic pseudocyst underwent reexaminations by B-ultrasonography.

The secondary observations were post-ERCP complications[20]. Post-ERCP pancreatitis (PEP), bleeding, infection, and perforation are the most common complications. PEP was defined as new or worsening abdominal pain with elevated blood amylase three times above the normal value and lasting longer than 24 h. Bleeding was defined as bleeding foci or persistent oozing of blood that was visible to the naked eye during the operation and vomiting of blood, blood in stool, or black stool with a progressive decrease in hemoglobin after the operation. Infection was defined as a postoperative temperature greater than 38°C and lasting for more than 24 h. Perforation was characterized by sudden abdominal pain and signs related to peritonitis during or after the operation. This included signs such as subdiaphragmatic free gas and retroperitoneal gas on imaging.

RESULTS

Basic clinical information

Among the ten children, there were five males and five females (age range: 4–13 years). There were nine cases at moderate risk and one case at low risk. All ten children showed recurrent abdominal pain and vomiting and were unable to eat. Among them, seven were fed through nasal jejunal tubes. The number of pancreatitis onsets before the operation was equal to or greater than two times. The weight loss before the operation was 2–7 kg. The time from the first AAP onset to ERCP was 3–8 mo (Table 1).

Status of ERCP operation

There were five cases of pseudocyst (5/10, 50%), six cases of pancreatic duct stones (6/10, 60%), and four cases of pancreatic duct stenosis (4/10, 40%). A total of seven cases (7/10, 70%) underwent pancreatic duct stent implantation; eight cases (8/10, 80%) underwent sphincterotomy; and five cases (5/10, 50%) had balloon manipulation. In total, two patients underwent ERCP operations twice for stent removal, while the remaining eight patients underwent only one operation (Table 2).

Status after ERCP

Among the five cases of pseudocyst, the cyst disappeared in four cases; no changes were observed in the cyst in one case even following the operation, but no pancreatitis occurred. After ERCP was performed, one patient developed three pancreatitis onsets due to continuous administration of ASP, but eating was not affected. The remaining nine patients did not develop pancreatitis after the operation and could eat normally. Weights increased by 1.5–8 kg across all patients.

After ERCP, one case developed mild pancreatitis, which recovered after medication. Moreover, two children developed postoperative infections but recovered after receiving anti-infective treatment (Table 3).

Table 1 Preoperative data of ten children

Case	Sex	Age (yr)	Risk grading	Interval between first AAP onset and ERCP (mo)	Clinical features	Nasal jejunal tube	Number of AAP onsets (times)	Weight loss (kg)
1	Female	4	Medium	4	Abdominal pain, vomiting, inability to eat	Yes	6	2
2	Male	10	Medium	3	Abdominal pain, vomiting, inability to eat	Yes	4	6
3	Male	12	Medium	3	Abdominal pain, vomiting, inability to eat	Yes	7	7
4	Male	6	Low	6	Abdominal pain, vomiting, inability to eat	Yes	9	4
5	Female	13	Medium	3	Abdominal pain, vomiting, inability to eat	Yes	5	2
6	Male	4	Medium	3	Abdominal pain, vomiting, inability to eat	No	5	3
7	Female	4	Medium	6	Abdominal pain, vomiting, inability to eat	Yes	9	3
8	Male	7	Medium	3	Abdominal pain, inability to eat	Yes	2	7
9	Female	7	Medium	8	Abdominal pain, vomiting, inability to eat	No	9	3
10	Female	4	Medium	4	Abdominal pain, vomiting, inability to eat	No	5	3

AAP: Asparaginase-associated pancreatitis; ERCP: Endoscopic retrograde cholangiopancreatography.

Table 2 Status of endoscopic retrograde cholangiopancreatography operation

Case	Presence of pseudocyst and its size (mm)	Pancreatic duct stenosis	Pancreatic duct stones	ERCP operation mode	ERCP operation times
1	40 × 15	No	Yes	EPS+ERPD	2
2	/	No	Yes	EPS+balloon manipulation	1
3	81 × 41	Yes	No	Balloon manipulation +ERPD	1
4	/	Yes	Yes	EPS+ERPD	2
5	68 × 40	Yes	No	Balloon manipulation+EPS+ERPD	1
6	16 × 12	No	No	EST	1
7	/	No	Yes	Balloon manipulation+ERPD	1
8	48 × 40	Yes	No	Balloon manipulation+EPS+ERPD	1
9	/	No	Yes	EPS	1
10	/	No	Yes	EPS+ERPD	1

EPS: Endoscopic pancreatography sphincterotomy; EST: Endoscopic sphincterotomy; ERPD: Endoscopic retrograde pancreatic drainage; ERCP: Endoscopic retrograde cholangiopancreatography.

DISCUSSION

AAP is a serious adverse reaction to ASP and is the most common reason for interruption of ASP treatment[21-23]. AAP is defined as an acute inflammatory process within the pancreatic parenchyma following ASP treatment. The diagnosis is based on the presence of at least two of the following three criteria: Abdominal pain suggestive of pancreatitis, serum amylase or lipase three or more times the upper-normal level, and characteristic imaging findings suggestive of pancreatitis. The underlying pathophysiology is not fully understood, but is thought to involve the reduction of protein synthesis, especially in organs with high protein turnover, such as the liver and pancreas, and results from systemic

Table 3 Follow-up data of the seven children

Case	Ultrasonography for pseudocyst	After ERCP acute pancreatitis onsets (times)	Clinical symptoms	Postoperative complications	Weight gain/yr (kg)
1	At 6 mo after the operation, no pseudocyst was found by ultrasonography	0	Abdominal pain disappeared, able to eat	No	5
2	/	0	Abdominal pain disappeared, able to eat	Postoperative pancreatitis	5
3	At 3 mo after the operation, no pseudocyst was found by ultrasonography	0	Abdominal pain disappeared, able to eat	Infection	8
4	/	0	Abdominal pain disappeared, able to eat	Infection	7
5	At 4 mo after the operation, ultrasonography revealed that the pseudocyst had disappeared	0	Abdominal pain disappeared, able to eat	No	3
6	There was still a 16 mm × 12 mm pseudocyst	0	Abdominal pain disappeared, able to eat	No	7
7	/	0	Abdominal pain disappeared, able to eat	No	1.5
8	At 2 mo after the operation, no pseudocyst was found by ultrasonography	0	Abdominal pain disappeared, able to eat	No	2
9	/	3	Abdominal pain, but did not affect eating	No	2
10	/	0	Abdominal pain disappeared, able to eat	No	3

ERCP: Endoscopic retrograde cholangiopancreatography.

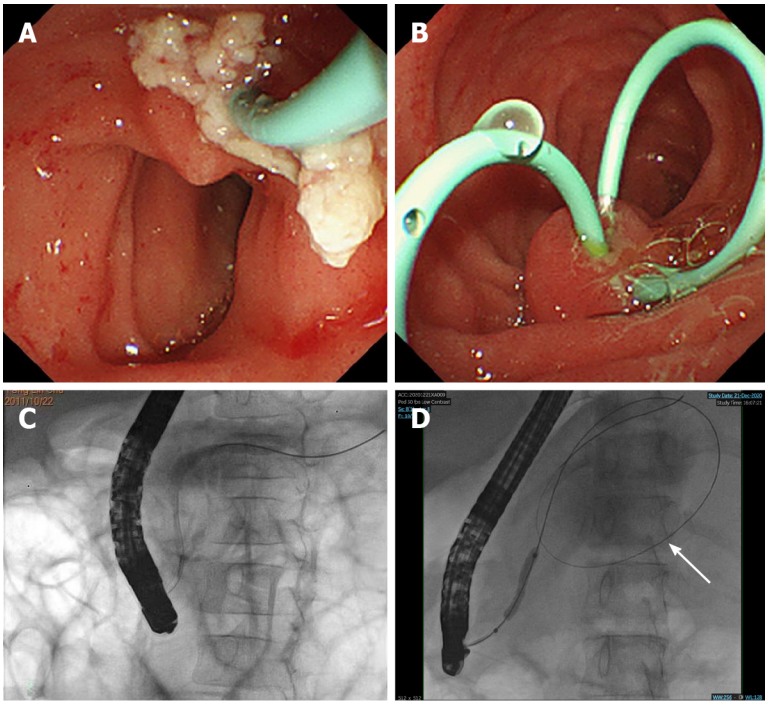
depletion of asparagine[19,24]. The Ponte di Legno consortium classified AAP into three grades according to the degree of pancreatic injury[19]. On the basis of severe pancreatitis, repeated pancreatitis is a high-risk factor for chronic pancreatitis. In addition, recurrent onsets of pancreatitis lead to children's inability to eat normally during chemotherapy, causing inadequate nutrition. Combined with the impact of chemotherapy drugs, this results in weight loss and insufficient immunity, seriously impacting children's quality of life.

In our study, ten children with AAP experienced recurrent pancreatitis presenting as abdominal pain, vomiting, inability to eat normally, and weight loss. Although seven patients had been placed on nasal jejunal tube feeding, their weight was still below the ideal due to recurrent pancreatitis. Therefore, once recurrent pancreatitis appears in AAP, intervention is necessary as early as possible to improve the quality of life of children and prevent chronic pancreatitis in the long term. However, most human clinical studies have focused on how to treat acute pancreatitis rather than relapsing pancreatitis.

ERCP is an endoscopic technique that combines gastrointestinal endoscopy and fluoroscopy for the diagnosis and treatment of pancreatic and biliary diseases. The application of ERCP in children has been increasing in recent years and its efficacy and safety have been demonstrated in operations such as sphincterotomy, papillary dilation, and pancreatic duct stenting. ERCP can safely be performed in children with a pooled complication rate of approximately 1.2-10.9%, paralleling that observed with adults[25,26].

Recurrent pancreatitis is a therapeutic indication for ERCP. Our study was comprised of ten children with recurrent pancreatitis related to ASP. Five had pancreatic pseudocyst, four had pancreatic duct stenosis, and six had pancreatic duct stones, suggesting that pseudocyst and pancreatic duct lesions were the root causes of recurrent pancreatitis and might even be the pathological basis of chronic pancreatitis. For pseudocyst and pancreatic duct lesions, medication is ineffective. ERCP is a minimally invasive treatment for biliary and pancreatic diseases in children, and symptomatic pancreatic pseudocyst and pancreatic duct diseases (stenosis and stones) are indications for ERCP[27-29]. Through pancreatic duct stent implantation, dilatation, and sphincterotomy, four cases of pseudocyst were resolved. Pseudocyst remained in one case, but no pancreatitis occurred; therefore, an observation strategy was maintained for natural absorption. A total of nine cases did not develop pancreatitis after the operation and the patients could, therefore, eat normally. Pancreatitis was observed in one case three times due to continuous use of ASP; however, the abdominal pain was mild and did not affect eating. The patient recovered after medication. All ten children gained weight after the operation. Two of the children developed an infection but recovered after anti-infective treatment. This supports ERCP as an effective and safe intervention for AAP with recurrent pancreatitis.

Pancreatic duct stones (PDS) are stones formed in the main pancreatic duct and pancreatic duct branches. They are a manifestation of protein embolism or mineralization (caused by calcium carbonate or protein in the pancreas precipitating in the pancreatic ducts) and are characteristic pathological changes of chronic pancreatitis. PDS and pancreatitis are mutually causal. Recurrent pancreatitis leads to increased secretion of pancreatic juice and the activation and concen-



DOI: 10.4253/wjge.v15.i10.614

Figure 1 Endoscopic retrograde cholangiopancreatography procedures. A: Endoscopic view of stone extraction; B: Endoscopic view showing that two pancreatic stents were placed after stone extraction; C: Fluoroscopic view of endoscopic retrograde cholangiopancreatography showing the dilated and tortuous pancreatic duct; D: Fluoroscopic view of pancreatic duct stricture dilation performed by balloon manipulation. White arrow shows the guide wire coiled inside the pseudocyst.

tration of a large amount of trypsinogen in the pancreatic ducts, leading to the formation of pancreatic stones. PDS block the pancreatic ducts, causing stenosis or dilation of the pancreatic ducts and subsequent recurrent pancreatitis[30]. In this study, six children were found to have PDS during the ERCP operation, and the cause of their formation might be related to the recurrence of pancreatitis after using ASP.

Approximately 23% of AAP episodes resulted in pancreatic pseudocyst, a markedly higher proportion than reported in a case series of pancreatitis due to all etiologies, which ranged from 2% to 16%[31]. Pancreatic pseudocyst is a common complication of pancreatitis that can manifest with abdominal symptoms of pain, nausea, and vomiting; it can also present without any clinical symptoms. Approximately 20%–60% of pancreatic pseudocysts naturally resolve within 6–12 wk[32,33]; therefore, ERCP is not the first treatment choice. When pancreatic pseudocysts are symptomatic, endoscopic intervention should be the therapy of first choice. In this study, the five cases of pseudocysts presented with recurrent pancreatitis. We observed these for at least 3 mo during which time the pseudocysts were still not absorbed. Furthermore, the children lost weight while waiting for the pseudocysts to be naturally absorbed. Therefore, once pancreatic pseudocysts with recurrent pancreatitis are present, we recommend ERCP treatment as early as possible.

In one case (case 9), where AAP recurred even after the ASP dosage was reduced by half, ERCP operation was performed to enable subsequent ASP treatment. After the operation, the child continued to receive three injections of ASP. Although there were still onsets of pancreatitis, compared with that before the operation, the number of onsets was reduced, degree of abdominal pain was alleviated, and eating was not affected. We believe that the implantation of a pancreatic duct stent is the key to ensuring successful chemotherapy with ASP. Meta-analysis data of many clinical reports show that stent placement could effectively relieve the symptoms of abdominal pain, with immediate relief rates of 65%–95% and sustained relief rates of 32%–68%[34]. Moreover, pancreatic duct stents could prevent post-ERCP pancreatitis in high-risk patients. Therefore, in the majority of patients (seven out of ten) in the study, a pancreatic duct stent was implanted, effectively relieving abdominal pain and, in the ninth case, protecting the pancreas from the damage caused by repeated ASP use. Repeated use of ASP in severe AAP is not typically recommended because up to 63% of children had a second recurrence of pancreatitis[5]. Based on our experience of using ERCP treatment in the ninth case, we believe that ERCP can be attempted in children with AAP prior to resuming the use of ASP to ensure that patients can complete their ASP treatment course, thereby improving the event-free survival rate in cases of ALL where children's ASP therapy is interrupted. To our knowledge, the efficacy and safety of ERCP in recurrent pancreatitis of ASP in children has not been reported to date. This is the largest number reported in China, with further detail than has previously been reported.

There are several limitations in the present study. First, this was a single-center and retrospective study with potential biases in inclusion criteria. Second, the sample size is notably limited due to the technically demanding and less commonly available nature of the ERCP procedure in most hospitals. The prevalent approach for cases of recurrent pancreatitis post-AAP prioritizes fluid replacement therapy, nutrition, and pain management. Additionally, it is important to note that ERCP is still in the process of development and refinement, especially concerning its application

for children with leukemia. Third, there was no control group in our study. Fourth, due to the underdeveloped nature of the rural area from which the patients originated, access to hospital resources is limited. This limitation could potentially contribute to the onset of pancreatitis, abdominal pain, vomiting, and weight gain among the patients. Finally, our study has a relatively short follow-up duration, averaging 1.2 years. This shorter duration may also impact the results of ERCP in AAP.

CONCLUSION

In summary, for AAP complicated by recurrent pancreatitis with pancreatic pseudocyst and pancreatic duct lesions (stones, pancreatic duct stenosis, or dilatation), ERCP appears to be an effective and safe intervention. Furthermore, ERCP seems to have a protective effect against pancreatic injury caused by repeated use of ASP. As a consequence, these patients can rapidly resume chemotherapy, which improves their outcome with regard to the underlying malignant disease.

ARTICLE HIGHLIGHTS

Research background

Asparaginase (ASP) is an important drug in combined chemotherapy regimens for pediatric acute lymphoblastic leukemia (ALL); ASP-associated pancreatitis (AAP) is the main adverse reaction of ASP. Recurrent pancreatitis is a complication of AAP, for which medication is ineffective.

Research motivation

As repeated occurrence of AAP limits the application of chemotherapy regimens for ALL, an effective, less invasive, and safe treatment strategy for AAP is desirable.

Research objectives

To evaluate the efficacy and safety of endoscopic retrograde cholangiopancreatography (ERCP) in treating recurrent pancreatitis due to AAP.

Research methods

From May 2018 to August 2021, ten children (five males and five females; age range: 4–13 years) with AAP were treated using ERCP due to recurrent pancreatitis. Clinical data of the ten children were collected, including their sex, age, weight, ALL risk grading, clinical symptoms at the onset of pancreatitis, time from the first pancreatitis onset to ERCP, ERCP operation status, and postoperative complications. The symptomatic relief, weight change, and number of pancreatitis onsets before and after ERCP were compared.

Research results

The preoperative symptoms were abdominal pain, vomiting, inability to eat, weight loss of 2–7 kg, and 2–9 pancreatitis onsets. After the operation, nine of ten patients did not develop pancreatitis, had no abdominal pain, could eat normally; the remaining patient developed three pancreatitis onsets due to continuous administration of ASP, but eating was not affected. The postoperative weight gain was 1.5–8 kg. There was one case of postoperative pancreatitis and two cases of postoperative infections; all recovered after medication.

Research conclusions

ERCP could improve clinical symptoms and reduce the incidence of pancreatitis, and was shown to be a safe and effective method for improving the management of recurrent pancreatitis of AAP.

Research perspectives

Based on our experience of using ERCP in treating recurrent pancreatitis due to AAP, we believe that ERCP can be attempted in children with AAP prior to resuming the use of ASP to ensure that patients can complete their ASP treatment course, thereby improving the event-free survival rate in cases of ALL where children's ASP therapy is interrupted.

FOOTNOTES

Author contributions: Yang KH, Zeng JQ, Ding S contributed equally to this work and share first authorship; Gong B and Deng ZH designed the study; Yang KH, Ding S, Zhang TA, Wang WY, Zhang JY, Wang L, Jian X acquired, analyzed, and interpreted the data; Yang KH and Zeng JQ drafted the manuscript; Deng ZH edited the manuscript; All authors contributed to the article and approved the submitted version.

Supported by the Science and Technology Commission of Shanghai Municipality of China, No. 22Y11921800.

Institutional review board statement: This study has been approved by the Institutional Ethnic Committee.

Informed consent statement: All study participants, or their legal guardian, provided written consent prior to study enrollment.

Conflict-of-interest statement: All the authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Data sharing statement: All individual data will shared. The data will be made available from the corresponding author (E-mail: dzhrj@163.com), upon reasonable request.

Country/Territory of origin: China

ORCID number: Kai-Hua Yang 0000-0002-1389-9137; Jing-Qing Zeng 0000-0002-7064-6662; Sheng Ding 0009-0007-8730-0979; Tian-Ao Zhang 0000-0002-8939-2244; Wen-Yu Wang 0000-0003-4118-1218; Jia-Yu Zhang 0000-0002-4553-2583; Lan Wang 0009-0004-4040-1623; Jian Xiao 0000-0002-3942-1924; Biao Gong 0000-0002-3645-2493; Zhao-Hui Deng 0000-0003-0780-9657.

S-Editor: Liu JH
L-Editor: Webster JR
P-Editor: Liu JH

REFERENCES

1 **Abu-El-Haija M**, Hornung L, Lin TK, Nathan JD, Thompson T, Vitale DS, Nasr A, Husain SZ, Denson L. Drug induced pancreatitis is the leading known cause of first attack acute pancreatitis in children. *Pancreatology* 2020; **20**: 1103-1108 [PMID: 32800650 DOI: 10.1016/j.pan.2020.07.008]

2 **Meczker Á**, Hanák L, Párniczky A, Szentesi A, Erőss B, Hegyi P; Hungarian Pancreatic Study Group. Analysis of 1060 Cases of Drug-Induced Acute Pancreatitis. *Gastroenterology* 2020; **159**: 1958-1961.e8 [PMID: 32687926 DOI: 10.1053/j.gastro.2020.07.016]

3 **Oparaji JA**, Rose F, Okafor D, Howard A, Turner RL, Orabi AI, Byersdorfer C, Mi Q, Ritchey K, Lowe ME, Husain SZ. Risk Factors for Asparaginase-associated Pancreatitis: A Systematic Review. *J Clin Gastroenterol* 2017; **51**: 907-913 [PMID: 28375864 DOI: 10.1097/MCG.0000000000000827]

4 **Rank CU**, Wolthers BO, Grell K, Albertsen BK, Frandsen TL, Overgaard UM, Toft N, Nielsen OJ, Wehner PS, Harila-Saari A, Heyman MM, Malmros J, Abrahamsson J, Norén-Nyström U, Tomaszewska-Toporska B, Lund B, Jarvis KB, Quist-Paulsen P, Vaitkevičienė GE, Griškevičius L, Taskinen M, Wartiovaara-Kautto U, Lepik K, Punab M, Jónsson ÓG, Schmiegelow K. Asparaginase-Associated Pancreatitis in Acute Lymphoblastic Leukemia: Results From the NOPHO ALL2008 Treatment of Patients 1-45 Years of Age. *J Clin Oncol* 2020; **38**: 145-154 [PMID: 31770057 DOI: 10.1200/JCO.19.02208]

5 **Stefanović M**, Jazbec J, Lindgren F, Bulajić M, Löhr M. Acute pancreatitis as a complication of childhood cancer treatment. *Cancer Med* 2016; **5**: 827-836 [PMID: 26872431 DOI: 10.1002/cam4.649]

6 **de Fine Licht S**, Winther JF, Gudmundsdottir T, Holmqvist AS, Bonnesen TG, Asdahl PH, Tryggvadottir L, Anderson H, Wesenberg F, Malila N, Holm K, Hasle H, Olsen JH; ALiCCS study group. Hospital contacts for endocrine disorders in Adult Life after Childhood Cancer in Scandinavia (ALiCCS): a population-based cohort study. *Lancet* 2014; **383**: 1981-1989 [PMID: 24556022 DOI: 10.1016/S0140-6736(13)62564-7]

7 **Kichler A**, Jang S. Chronic Pancreatitis: Epidemiology, Diagnosis, and Management Updates. *Drugs* 2020; **80**: 1155-1168 [PMID: 32647920 DOI: 10.1007/s40265-020-01360-6]

8 **Kumar S**, Ooi CY, Werlin S, Abu-El-Haija M, Barth B, Bellin MD, Durie PR, Fishman DS, Freedman SD, Gariepy C, Giefer MJ, Gonska T, Heyman MB, Himes R, Husain SZ, Lin TK, Lowe ME, Morinville V, Palermo JJ, Pohl JF, Schwarzenberg SJ, Troendle D, Wilschanski M, Zimmerman MB, Uc A. Risk Factors Associated With Pediatric Acute Recurrent and Chronic Pancreatitis: Lessons From INSPPIRE. *JAMA Pediatr* 2016; **170**: 562-569 [PMID: 27064572 DOI: 10.1001/jamapediatrics.2015.4955]

9 **Liu QY**, Abu-El-Haija M, Husain SZ, Barth B, Bellin M, Fishman DS, Freedman SD, Gariepy CE, Giefer MJ, Gonska T, Heyman MB, Himes R, Lin TK, Maqbool A, Mascarenhas M, McFerron BA, Morinville VD, Nathan JD, Ooi CY, Perito ER, Pohl JF, Rhee S, Schwarzenberg SJ, Shah U, Troendle D, Werlin SL, Wilschanski M, Zimmerman MB, Lowe ME, Uc A. Risk Factors for Rapid Progression From Acute Recurrent to Chronic Pancreatitis in Children: Report From INSPPIRE. *J Pediatr Gastroenterol Nutr* 2019; **69**: 206-211 [PMID: 31136562 DOI: 10.1097/MPG.0000000000002405]

10 **Sankaran SJ**, Xiao AY, Wu LM, Windsor JA, Forsmark CE, Petrov MS. Frequency of progression from acute to chronic pancreatitis and risk factors: a meta-analysis. *Gastroenterology* 2015; **149**: 1490-1500.e1 [PMID: 26299411 DOI: 10.1053/j.gastro.2015.07.066]

11 **Witt H**, Apte MV, Keim V, Wilson JS. Chronic pancreatitis: challenges and advances in pathogenesis, genetics, diagnosis, and therapy. *Gastroenterology* 2007; **132**: 1557-1573 [PMID: 17466744 DOI: 10.1053/j.gastro.2007.03.001]

12 **Felux J**, Sturm E, Busch A, Zerabruck E, Graepler F, Stüker D, Manger A, Kirschner HJ, Blumenstock G, Malek NP, Goetz M. ERCP in infants, children and adolescents is feasible and safe: results from a tertiary care center. *United European Gastroenterol J* 2017; **5**: 1024-1029 [PMID: 29163969 DOI: 10.1177/2050640616687868]

13 **Kohoutova D**, Tringali A, Papparella G, Perri V, Boškoski I, Hamanaka J, Costamagna G. Endoscopic treatment of chronic pancreatitis in pediatric population: Long-term efficacy and safety. *United European Gastroenterol J* 2019; **7**: 270-277 [PMID: 31080612 DOI: 10.1177/2050640618817699]

14 **Pan G**, Yang K, Gong B, Deng Z. Analysis of the Efficacy and Safety of Endoscopic Retrograde Cholangiopancreatography in Children With Symptomatic Pancreas Divisum. *Front Pediatr* 2021; **9**: 761331 [PMID: 34796156 DOI: 10.3389/fped.2021.761331]

15 **Poddar U**, Yachha SK, Borkar V, Srivastava A, Saraswat VA. Clinical profile and treatment outcome of chronic pancreatitis in children: a long-term follow-up study of 156 cases. *Scand J Gastroenterol* 2017; **52**: 773-778 [PMID: 28276824 DOI: 10.1080/00365521.2017.1295465]

16 **Troendle DM**, Fishman DS, Barth BA, Giefer MJ, Lin TK, Liu QY, Abu-El-Haija M, Bellin MD, Durie PR, Freedman SD, Gariepy C, Gonska T, Heyman MB, Himes R, Husain SZ, Kumar S, Lowe ME, Morinville VD, Ooi CY, Palermo J, Pohl JF, Schwarzenberg SJ, Werlin S, Wilschanski M, Zimmerman MB, Uc A. Therapeutic Endoscopic Retrograde Cholangiopancreatography in Pediatric Patients With Acute Recurrent and Chronic Pancreatitis: Data From the INSPPIRE (INternational Study group of Pediatric Pancreatitis: In search for a cuRE) Study. *Pancreas* 2017; **46**: 764-769 [PMID: 28609364 DOI: 10.1097/MPA.0000000000000848]

17 **Xue N**, Lei XF, Xu JJ, Wei XX. [Progression of endoscopic retrograde cholangiopancreatography in children with pancreaticobiliary diseases]. *Zhonghua Er Ke Za Zhi* 2021; **59**: 145-149 [PMID: 33548965 DOI: 10.3760/cma.j.cn112140-20200618-00633]

18 **Párniczky A**, Abu-El-Haija M, Husain S, Lowe M, Oracz G, Sahin-Tóth M, Szabó FK, Uc A, Wilschanski M, Witt H, Czakó L, Grammatikopoulos T, Rasmussen IC, Sutton R, Hegyi P. EPC/HPSG evidence-based guidelines for the management of pediatric pancreatitis. *Pancreatology* 2018; **18**: 146-160 [PMID: 29398347 DOI: 10.1016/j.pan.2018.01.001]

19 **Schmiegelow K**, Attarbaschi A, Barzilai S, Escherich G, Frandsen TL, Halsey C, Hough R, Jeha S, Kato M, Liang DC, Mikkelsen TS, Möricke A, Niinimäki R, Piette C, Putti MC, Raetz E, Silverman LB, Skinner R, Tuckuviene R, van der Sluis I, Zapotocka E; Ponte di Legno toxicity working group. Consensus definitions of 14 severe acute toxic effects for childhood lymphoblastic leukaemia treatment: a Delphi consensus. *Lancet Oncol* 2016; **17**: e231-e239 [PMID: 27299279 DOI: 10.1016/S1470-2045(16)30035-3]

20 **Cotton PB**, Lehman G, Vennes J, Geenen JE, Russell RC, Meyers WC, Liguory C, Nickl N. Endoscopic sphincterotomy complications and their management: an attempt at consensus. *Gastrointest Endosc* 1991; **37**: 383-393 [PMID: 2070995 DOI: 10.1016/S0016-5107(91)70740-2]

21 **Baruchel A**, Brown P, Rizzari C, Silverman L, van der Sluis I, Wolthers BO, Schmiegelow K. Increasing completion of asparaginase treatment in childhood acute lymphoblastic leukaemia (ALL): summary of an expert panel discussion. *ESMO Open* 2020; **5**: e000977 [PMID: 32967920 DOI: 10.1136/esmoopen-2020-000977]

22 **Hijiya N**, van der Sluis IM. Asparaginase-associated toxicity in children with acute lymphoblastic leukemia. *Leuk Lymphoma* 2016; **57**: 748-757 [PMID: 26457414 DOI: 10.3109/10428194.2015.1101098]

23 **Kearney SL**, Dahlberg SE, Levy DE, Voss SD, Sallan SE, Silverman LB. Clinical course and outcome in children with acute lymphoblastic leukemia and asparaginase-associated pancreatitis. *Pediatr Blood Cancer* 2009; **53**: 162-167 [PMID: 19405141 DOI: 10.1002/pbc.22076]

24 **Wolthers BO**, Frandsen TL, Baruchel A, Attarbaschi A, Barzilai S, Colombini A, Escherich G, Grell K, Inaba H, Kovacs G, Liang DC, Mateos M, Mondelaers V, Möricke A, Ociepa T, Samarasinghe S, Silverman LB, van der Sluis IM, Stanulla M, Vrooman LM, Yano M, Zapotocka E, Schmiegelow K; Ponte di Legno Toxicity Working Group. Asparaginase-associated pancreatitis in childhood acute lymphoblastic leukaemia: an observational Ponte di Legno Toxicity Working Group study. *Lancet Oncol* 2017; **18**: 1238-1248 [PMID: 28736188 DOI: 10.1016/S1470-2045(17)30424-2]

25 **Troendle DM**, Abraham O, Huang R, Barth BA. Factors associated with post-ERCP pancreatitis and the effect of pancreatic duct stenting in a pediatric population. *Gastrointest Endosc* 2015; **81**: 1408-1416 [PMID: 25686874 DOI: 10.1016/j.gie.2014.11.022]

26 **Keil R**, Drábek J, Lochmannová J, Šťovíček J, Koptová P, Wasserbauer M, Frýbová B, Šnajdauf J, Matouš J, Kotalová R, Rygl M, Hlava Š. ERCP in infants, children, and adolescents-Different roles of the methods in different age groups. *PLoS One* 2019; **14**: e0210805 [PMID: 30653580 DOI: 10.1371/journal.pone.0210805]

27 **Dumonceau JM**, Delhaye M, Tringali A, Arvanitakis M, Sanchez-Yague A, Vaysse T, Aithal GP, Anderloni A, Bruno M, Cantú P, Devière J, Domínguez-Muñoz JE, Lekkerkerker S, Poley JW, Ramchandani M, Reddy N, van Hooft JE. Endoscopic treatment of chronic pancreatitis: European Society of Gastrointestinal Endoscopy (ESGE) Guideline - Updated August 2018. *Endoscopy* 2019; **51**: 179-193 [PMID: 30654394 DOI: 10.1055/a-0822-0832]

28 **Freeman AJ**, Maqbool A, Bellin MD, Goldschneider KR, Grover AS, Hartzell C, Piester TL, Szabo F, Kiernan BD, Khalaf R, Kumar R, Rios M, Husain SZ, Morinville VD, Abu-El-Haija M. Medical Management of Chronic Pancreatitis in Children: A Position Paper by the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition Pancreas Committee. *J Pediatr Gastroenterol Nutr* 2021; **72**: 324-340 [PMID: 33230082 DOI: 10.1097/MPG.0000000000003001]

29 **Hart PA**, Conwell DL. Chronic Pancreatitis: Managing a Difficult Disease. *Am J Gastroenterol* 2020; **115**: 49-55 [PMID: 31764092 DOI: 10.14309/ajg.0000000000000421]

30 **Skipper MT**, Albertsen BK, Schmiegelow K, Andrés-Jensen L. Long-term effects of asparaginase-associated pancreatitis. *Pediatr Blood Cancer* 2023; e30528 [PMID: 37376950 DOI: 10.1002/pbc.30528]

31 **Dua MM**, Visser BC. Surgical Approaches to Chronic Pancreatitis: Indications and Techniques. *Dig Dis Sci* 2017; **62**: 1738-1744 [PMID: 28281166 DOI: 10.1007/s10620-017-4526-x]

32 **Lu X**, Uchida E, Yokomuro S, Nakamura Y, Aimoto T, Tajiri T. Features and choice of treatment of acute and chronic pancreatic pseudocysts--with special reference to invasive intervention. *Pancreatology* 2008; **8**: 30-35 [PMID: 18235214 DOI: 10.1159/000114853]

33 **Tan JH**, Chin W, Shaikh AL, Zheng S. Pancreatic pseudocyst: Dilemma of its recent management (Review). *Exp Ther Med* 2021; **21**: 159 [PMID: 33456526 DOI: 10.3892/etm.2020.9590]

34 **Adler JM**, Gardner TB. Endoscopic Therapies for Chronic Pancreatitis. *Dig Dis Sci* 2017; **62**: 1729-1737 [PMID: 28258377 DOI: 10.1007/s10620-017-4502-5]

World Journal of Gastrointestinal Endoscopy

Submit a Manuscript: https://www.f6publishing.com

World J Gastrointest Endosc 2023 October 16; 15(10): 623-628

DOI: 10.4253/wjge.v15.i10.623

ISSN 1948-5190 (online)

CASE REPORT

Polyposis found on index colonoscopy in a 56-year-old female - *BMPR1A* variant in juvenile polyposis syndrome: A case report

Michael Yulong Wu, Christopher Toon, Michael Field, May Wong

Specialty type: Gastroenterology and hepatology

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): B, B
Grade C (Good): C
Grade D (Fair): D
Grade E (Poor): 0

P-Reviewer: Kishikawa H, Japan; Sahin Y, Turkey; Zhang X, United States; Zhao ZY, China

Received: May 10, 2023
Peer-review started: May 10, 2023
First decision: July 9, 2023
Revised: July 21, 2023
Accepted: July 31, 2023
Article in press: July 31, 2023
Published online: October 16, 2023

Michael Yulong Wu, May Wong, Department of Gastroenterology and Hepatology, Royal North Shore Hospital, Sydney 2065, New South Wales, Australia

Michael Yulong Wu, May Wong, Northern Clinical School, The University of Sydney, Sydney 2065, New South Wales, Australia

Christopher Toon, NSW Health Pathology, Department of Anatomical Pathology, Royal North Shore Hospital, Sydney 2065, New South Wales, Australia

Michael Field, Clinical Genetics, Royal North Shore Hospital, Sydney 2065, New South Wales, Australia

Corresponding author: Michael Yulong Wu, MD, Doctor, Department of Gastroenterology and Hepatology, Royal North Shore Hospital, 1 Reserve Road, Sydney 2065, New South Wales, Australia. michaelyulong@gmail.com

Abstract

BACKGROUND

Juvenile polyposis syndrome (JPS) is a rare hereditary polyposis disease frequently associated with an autosomal-dominant variant of the *SMAD4* or *BMPR1A* gene. It often manifests with symptoms in children and adolescents and is infrequently diagnosed in asymptomatic adults. Establishing the diagnosis is important as patients with JPS have a high risk of developing gastrointestinal cancer and require genetic counselling and close routine follow-up.

CASE SUMMARY

We report on the case of a 56-year-old female diagnosed with JPS after genetic testing revealed a rare variant of the *BMPR1A* gene *BMPR1A c.1409T>C* (p.Met470Thr). She was initially referred for colonoscopy by her general practitioner after testing positive on a screening faecal immunochemical test and subsequently found to have polyposis throughout the entire colorectum on her index screening colonoscopy. The patient was asymptomatic with a normal physical examination and no related medical or family history. Blood tests revealed only mild iron deficiency without anemia. To date, there has only been one other reported case of JPS with the same genetic variant. Subsequent colonoscopies were organised for complete polyp clearance and the patient was returned for surveillance follow-up.

CONCLUSION

JPS patients can present with no prior symptoms or family history. Genetic testing plays an important diagnostic role guiding management.

Key Words: Juvenile polyposis syndrome; Polyps; Colorectal polyp; Hereditary polyposis; Cancer; Case report

Core Tip: Juvenile polyposis syndrome (JPS) is a hereditary autosomal dominant disease that phenotypically presents with polyposis throughout the colorectum. Detection and diagnosis is important as patients have a high risk of developing gastrointestinal cancer. Symptoms often manifest in childhood and adolescence with most having evidence of an associated family history. We report a case of polyposis found on index screening endoscopy in an asymptomatic female with no prior related family or medical history. Subsequent genetic testing led to the diagnosis of JPS after detecting a rare variant of the *BMPR1A* gene previously only reported in one other case of JPS.

Citation: Wu MY, Toon C, Field M, Wong M. Polyposis found on index colonoscopy in a 56-year-old female - *BMPR1A* variant in juvenile polyposis syndrome: A case report. *World J Gastrointest Endosc* 2023; 15(10): 623-628
URL: https://www.wjgnet.com/1948-5190/full/v15/i10/623.htm
DOI: https://dx.doi.org/10.4253/wjge.v15.i10.623

INTRODUCTION

Hereditary gastrointestinal polyposis syndromes are a rare group of diseases that account for up to approximately 5% of all colorectal cancers[1]. These polyposis syndromes are broadly categorised based on whether polyps demonstrate predominantly adenomatous or hamartomatous changes. Hamartomatous polyposis syndromes include Peutz-Jeghers syndrome, phosphatase and tensin homolog (PTEN) hamartomatous syndromes (Cowden syndrome and PTEN-related Proteus syndromes) and Juvenile Polyposis syndrome (JPS)[2]. Early recognition and detection of these hereditary diseases is important due to the lifetime risk of developing gastrointestinal cancer. JPS often manifests with gastrointestinal symptoms such as rectal bleeding, anemia, bowel habit changes and abdominal pain in childhood with an average age of diagnosis in the adolescent years[3,4]. We present a case of a patient with polyposis found on index screening endoscopy and discovery of a rare *de novo* variant of the *BMPR1A* gene on genetic testing leading to the subsequent diagnosis of JPS. This is a unique presentation of an asymptomatic adult with no related medical or family history and to date, there has been only one other reported case of JPS with the same genetic variant. This case highlights the importance of clinician vigilance as many individuals may present with no related history and emphasises the need for early genetic testing to guide appropriate management and surveillance intervals.

CASE PRESENTATION

Chief complaints

A 56-year-old female was referred in by her general practitioner after she tested positive on screening faecal immunochemical test.

History of present illness

She reported some infrequent constipation but no acute bowel habit changes. Overall, she was constitutionally well with no history of abdominal pain, malaena, haematochezia, or weight loss.

History of past illness

She had a medical history of gastroesophageal reflux disease and asthma. Her only regular medication was a budesonide-formoterol (200 mcg/6 mcg) inhaler.

Personal and family history

She had no history of smoking or alcohol use. There was no family history of colorectal cancer or other gastrointestinal diseases.

Physical examination

The patient was fit and well with normal vital signs. There were no significant findings on physical examination such as skin lesions commonly associated with Cowden and other PTEN hamartoma syndromes, mucosal pigmentation associated with Peutz-Jeghers syndrome and macrocephaly associated with JPS[5-7]. There were no features of alopecia,

onychodystrophy or hyperpigmentation that may be seen in Cronkhite-Canada syndrome[8]. She had no features of Hereditary Haemorrhagic Telangectasia typically seen in *SMAD4* juvenile polyposis.

Laboratory examinations

The only abnormalities on her blood tests were a mild iron deficiency with ferritin level 25 μg/L (reference range 30–300 μg/L) without anaemia.

Imaging examinations

The patient proceeded to a gastroscopy which found a single medium-sized fundic gland polyp and a colonoscopy demonstrating more than one hundred pedunculated polyps throughout the caecum, ascending colon, transverse colon, descending colon, sigmoid colon, rectosigmoid colon and rectum (Figure 1). Initial biopsies were taken throughout the gastrointestinal tract and several larger polyps were removed for histology. A computed tomography enterography of the small bowel did not show any small bowel polyps.

FURTHER DIAGNOSTIC WORK-UP

On histology, the polypoid colonic mucosa showed epithelial-stromal hamartomatous features with variable epithelial hyperplasia and subtle myofibroblastic proliferation in the lamina propria (Figure 2). Overall features were consistent with a hamartomatous polyposis syndrome. JPS, Peutz-Jegher syndrome, Cronkhite-Canada syndrome and Cowden syndrome were considered differential diagnoses however sub-classification proved difficult as there were no further distinguishing histological features[9,10].

The patient was referred for multi-gene panel testing which included *STK11* associated with Peutz-Jeghers syndrome, *PTEN* associated with PTEN hamartoma syndromes (Cowden syndrome and PTEN-related Proteus syndromes) and *SMAD4* and *BMPR1A* associated with JPS. Massively Parallel Sequencing of > 99% of the coding sequences including the exon/intron boundaries to a depth of > 200 was performed to generate this result. SOPHiA genetics DDM (Sophia Genetics, Saint-Sulpice, Switzerland) was used to generate aligned reads and call variants against the hg19 human reference genome. A rare variant of *BMPR1A* written as *BMPR1A c.1409T>C* (p.Met470Thr) was identified and JPS was diagnosed as the likely cause of her polyposis phenotype. The patient has three siblings and one surviving parent none of whom have a history of colorectal cancer or polyps. All bar one of these relatives lives overseas. The patient's 35-year-old son subsequently underwent a colonoscopy which showed no polyps. Genetic testing was also offered to the son which returned negative for the *BMPR1A* variant.

FINAL DIAGNOSIS

The combination of colonoscopy findings, histopathology and multi-gene panel testing led to the diagnosis of JPS.

TREATMENT

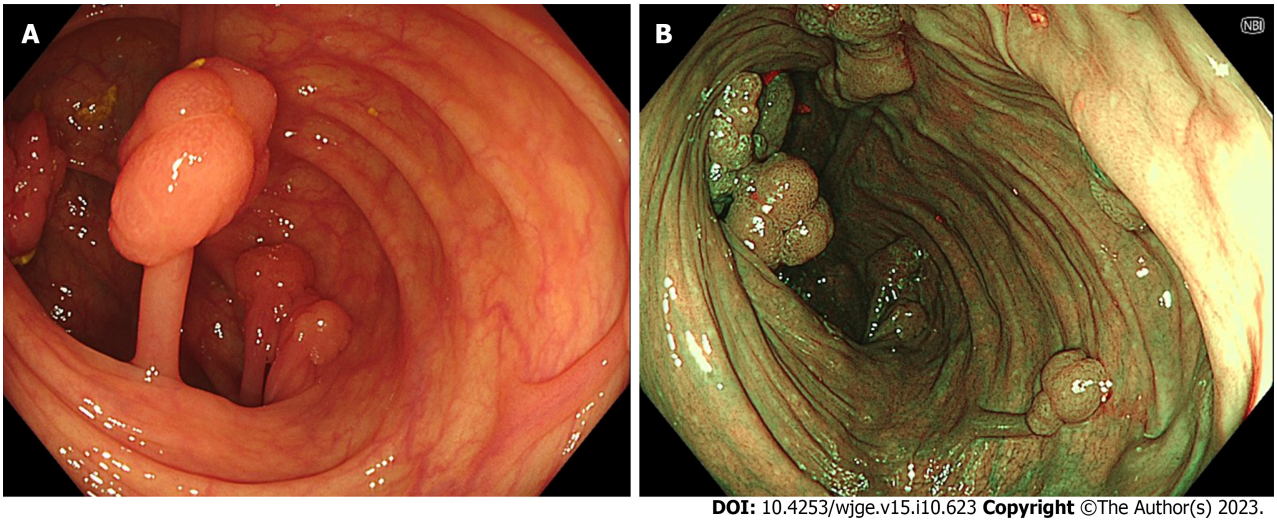
Three subsequent colonoscopies were organised for complete polyp clearance and histopathology demonstrated similar hamartomatous polyps with some showing early adenomatous changes.

OUTCOME AND FOLLOW-UP

The patient was recommended to return for yearly colonoscopy surveillance given the initial polyp burden.

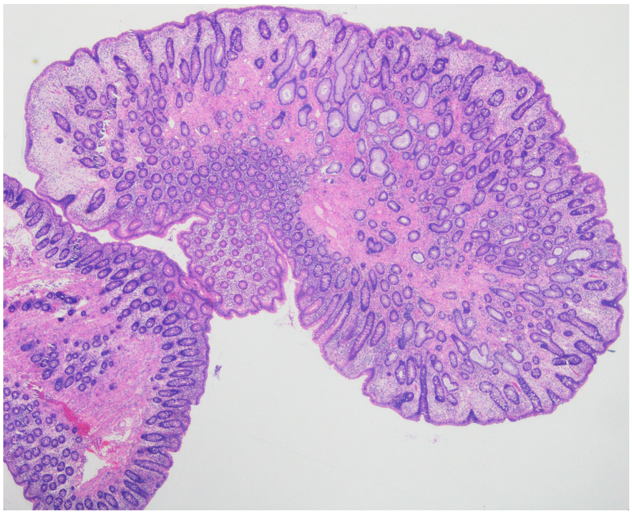
DISCUSSION

JPS is a rare autosomal dominant disease with an estimated incidence around 1/100000–1/160000 and a 39%-68% lifetime risk of colon cancer[11]. Polyp growth occurs primarily in the colorectum but can also appear in the stomach and small bowel. Macroscopically JPS polyps appear as pedunculated, exophytic, shiny and spherical growths[2,12]. Histologically, juvenile polyps typically demonstrate dilated thick mucin-filled glands with inflammatory infiltrates in the lamina propria. Despite these features, polyps in JPS can often still be indistinguishable from other polyposis syndromes. Clinical diagnostic criteria also exist in which a diagnosis can be made with the presence of any of the following: > 5 juvenile polyps in the colorectum, juvenile polyps in other parts of the gastrointestinal tract or any number of juvenile polyps and a positive family history[13]. Confirmatory genetic testing is recommended for all patients meeting clinical diagnostic criteria however the presence of germline mutations may only be present in 20%-60% of individuals[4,12]. Making an accurate diagnosis of JPS can remain a challenge for clinicians due to the similarity of features with other polyposis



DOI: 10.4253/wjge.v15.i10.623 **Copyright** ©The Author(s) 2023.

Figure 1 Endoscopic view. A and B: White Light Endoscopy Transverse Colon (A) and Narrow Band Imaging Transverse colon (B) showing pedunculated polyps in the transverse colon with some grouped into grapelike clusters.



DOI: 10.4253/wjge.v15.i10.623 **Copyright** ©The Author(s) 2023.

Figure 2 Histology of ascending colon polyp.

syndromes and a lack of a clear 'gold standard' diagnostic. In our case, a diagnosis was made on the basis of polyp morphology, histology and confirmatory genetic testing.

The heterozygous *BMPR1A c.1409T>C* (p.Met470Thr) variant is a missense mutation of Methionine to Threonine and identified only in one other patient with JPS[14]. In silico analysis predicted the variant affects protein function. Based on a lack of functional proof and biological information that the variant was damaging, the variant was classified as a variant of unclear significance (class 3) according to the American College of Medical Genetics and Genomics-Association for Molecular Pathology SHERLOC guidelines[15]. Whilst 45% to 60% of JPS cases are attributed to more common diease-causing variants in either the *BMPR1A* or *SMAD4* gene, there are still a number of cases without an identifiable pathogenic variant[16]. Since the variant is absent in a large population control group (gnomAD), has been previously reported in a patient with JPS and showed limited segregation with disease in this family, the *BMPR1A c.1409T>C* (p.Met470Thr) variant was considered by the authors to be the likely cause of the patients phenotype[17]. Given the rarity of disease, reporting on the polyposis features of this patient diagnosed with JPS contributes to the growing body of knowledge on the pathogenecity of *BMPR1A* variants.

The role of genetic counselling is invaluable in the management of a patient with JPS. Around 50% of individuals with JPS will have affected parents whilst the remaining half will have no prior family history of polyps and represent a *de novo* mutation[18]. Children of affected individuals have a 50% chance of inheritance. It is recommended that even asymptomatic relatives of individuals with JPS undergo evaluations with either genetic testing, if the gene variant is known, or endoscopic screening if the variant is unknown[18]. In the case of this patient, genetic screening was performed on the son to ensure early disease surveillance and monitoring.

For patients with polyposis syndrome, current guidelines by the American College of Gastroenterology (ACG) recommend screening gastroscopy and colonoscopy from age 12 or earlier if individuals are symptomatic with repeat surveillance endoscopy every 1–3 years depending on polyp burden[4]. The European Society of Gastrointestinal Endoscopy (ESGE) outline similar colonoscopy age intervals however recommend gastroscopy in asymptomatic individuals start at 18 years for those with a *SMAD4* mutation and at 25 years in those with *BMPR1A* mutation[19]. The ACG recommends removal of all polyps ≥ 5 mm whilst the ESGE recommends removal of those > 10 mm[4,19]. Periodic surveillance of the small bowel is recommended by the ACG however is not recommended by the ESGE given the rarity of small bowel involvement in JPS[4,19]. Surgical management with colectomy and ileo-rectal anastomosis is recommended if cancer, high-grade dysplasia or polyposis cannot be managed endoscopically[4]. In our patient, serial colonoscopies at 3 monthly intervals were adequate for complete polyp clearance and follow-up was organised for yearly surveillance given the significant polyp burden on initial colonoscopy. Current guidelines provide blanket recommendations to all patients diagnosed with JPS regardless of the gene-phenotype. Therefore a better understanding of the pathogenecity of gene variants can provide information that may help individualise clinical surveillance intervals.

This case highlights the presentation of an asymptomatic female found to have a rare potentially *de novo* variant in the *BMPR1A* gene leading to the diagnosis of JPS. This case serves as a reminder that many patients may be asymptomatic with no related medical or family history. It demonstrates the importance of referral to a geneticist for multigene panel testing for confirmatory diagnosis, guidance on further management of the patient and cancer surveillance intervals.

CONCLUSION

JPS is a rare disease that can be a challenging diagnosis to be distinguished from other hereditary polyposis syndromes. This case demonstrates that some patients may present in adulthood with no related symptoms or prior history. We describe the second reported case in literature of a rare potentially *de novo* variant of the *BMPR1A* gene in a patient with JPS. This report contributes to the developing body of literature and understanding in the pathogenicity of variants in *BMPR1A* gene.

FOOTNOTES

Author contributions: Wu MY and Wong M contributed to manuscript writing and editing; Toon C contributed to anatomical pathology analysis and manuscript editing; Field M contributed to genetic analysis and manuscript editing; All authors have read and approved the final manuscript.

Informed consent statement: Informed written consent was obtained from the patient for publication of this report and any accompanying images.

Conflict-of-interest statement: The authors declare no conflict-of-interests.

CARE Checklist (2016) statement: The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

Country/Territory of origin: Australia

ORCID number: Michael Yulong Wu 0000-0003-1659-8599; Christopher Toon 0000-0002-0750-918X; Michael Field 0000-0001-7455-934X; May Wong 0000-0003-2856-7327.

S-Editor: Lin C
L-Editor: A
P-Editor: Cai YX

REFERENCES

1 **Patel R**, Hyer W. Practical management of polyposis syndromes. *Frontline Gastroenterol* 2019; **10**: 379-387 [PMID: 31656563 DOI: 10.1136/flgastro-2018-101053]
2 **Aretz S**. The differential diagnosis and surveillance of hereditary gastrointestinal polyposis syndromes. *Dtsch Arztebl Int* 2010; **107**: 163-173 [PMID: 20358032 DOI: 10.3238/arztebl.2010.0163]
3 **Manfredi M**. Hereditary hamartomatous polyposis syndromes: understanding the disease risks as children reach adulthood. *Gastroenterol Hepatol (N Y)* 2010; **6**: 185-196 [PMID: 20567567]

4 **Syngal S**, Brand RE, Church JM, Giardiello FM, Hampel HL, Burt RW; American College of Gastroenterology. ACG clinical guideline: Genetic testing and management of hereditary gastrointestinal cancer syndromes. *Am J Gastroenterol* 2015; **110**: 223-62; quiz 263 [PMID: 25645574 DOI: 10.1038/ajg.2014.435]

5 **Beggs AD**, Latchford AR, Vasen HF, Moslein G, Alonso A, Aretz S, Bertario L, Blanco I, Bülow S, Burn J, Capella G, Colas C, Friedl W, Møller P, Hes FJ, Järvinen H, Mecklin JP, Nagengast FM, Parc Y, Phillips RK, Hyer W, Ponz de Leon M, Renkonen-Sinisalo L, Sampson JR, Stormorken A, Tejpar S, Thomas HJ, Wijnen JT, Clark SK, Hodgson SV. Peutz-Jeghers syndrome: a systematic review and recommendations for management. *Gut* 2010; **59**: 975-986 [PMID: 20581245 DOI: 10.1136/gut.2009.198499]

6 **Brosens LA**, Langeveld D, van Hattem WA, Giardiello FM, Offerhaus GJ. Juvenile polyposis syndrome. *World J Gastroenterol* 2011; **17**: 4839-4844 [PMID: 22171123 DOI: 10.3748/wjg.v17.i44.4839]

7 **Pilarski R**, Burt R, Kohlman W, Pho L, Shannon KM, Swisher E. Cowden syndrome and the PTEN hamartoma tumor syndrome: systematic review and revised diagnostic criteria. *J Natl Cancer Inst* 2013; **105**: 1607-1616 [PMID: 24136893 DOI: 10.1093/jnci/djt277]

8 **Sweetser S**, Ahlquist DA, Osborn NK, Sanderson SO, Smyrk TC, Chari ST; Boardman LA. Clinicopathologic features and treatment outcomes in Cronkhite-Canada syndrome: support for autoimmunity. *Dig Dis Sci* 2012; **57**: 496-502 [PMID: 21881972 DOI: 10.1007/s10620-011-1874-9]

9 **Kopáčová M**, Urban O, Cyrany J, Laco J, Bureš J, Rejchrt S, Bártová J, Tachecí I. Cronkhite-Canada syndrome: review of the literature. *Gastroenterol Res Pract* 2013; **2013**: 856873 [PMID: 24369458 DOI: 10.1155/2013/856873]

10 **Schreibman IR**, Baker M, Amos C, McGarrity TJ. The hamartomatous polyposis syndromes: a clinical and molecular review. *Am J Gastroenterol* 2005; **100**: 476-490 [PMID: 15667510 DOI: 10.1111/j.1572-0241.2005.40237.x]

11 **Kidambi TD**, Kohli DR, Samadder NJ, Singh A. Hereditary Polyposis Syndromes. *Curr Treat Options Gastroenterol* 2019; **17**: 650-665 [PMID: 31705372 DOI: 10.1007/s11938-019-00251-4]

12 **Zbuk KM**, Eng C. Hamartomatous polyposis syndromes. *Nat Clin Pract Gastroenterol Hepatol* 2007; **4**: 492-502 [PMID: 17768394 DOI: 10.1038/ncpgasthep0902]

13 **Latchford AR**, Neale K, Phillips RK, Clark SK. Juvenile polyposis syndrome: a study of genotype, phenotype, and long-term outcome. *Dis Colon Rectum* 2012; **55**: 1038-1043 [PMID: 22965402 DOI: 10.1097/DCR.0b013e31826278b3]

14 **Kim IJ**, Park JH, Kang HC, Kim KH, Kim JH, Ku JL, Kang SB, Park SY, Lee JS, Park JG. Identification of a novel BMPR1A germline mutation in a Korean juvenile polyposis patient without SMAD4 mutation. *Clin Genet* 2003; **63**: 126-130 [PMID: 12630959 DOI: 10.1034/j.1399-0004.2003.00008.x]

15 **Nykamp K**, Anderson M, Powers M, Garcia J, Herrera B, Ho YY, Kobayashi Y, Patil N, Thusberg J, Westbrook M; Invitae Clinical Genomics Group, Topper S. Sherloc: a comprehensive refinement of the ACMG-AMP variant classification criteria. *Genet Med* 2017; **19**: 1105-1117 [PMID: 28492532 DOI: 10.1038/gim.2017.37]

16 **Papadopulos ME**, Plazzer JP, Macrae FA. Genotype-phenotype correlation of BMPR1a disease causing variants in juvenile polyposis syndrome. *Hered Cancer Clin Pract* 2023; **21**: 12 [PMID: 37400896 DOI: 10.1186/s13053-023-00255-3]

17 **Karczewski KJ**, Francioli LC, Tiao G, Cummings BB, Alföldi J, Wang Q, Collins RL, Laricchia KM, Ganna A, Birnbaum DP, Gauthier LD, Brand H, Solomonson M, Watts NA, Rhodes D, Singer-Berk M, England EM, Seaby EG, Kosmicki JA, Walters RK, Tashman K, Farjoun Y, Banks E, Poterba T, Wang A, Seed C, Whiffin N, Chong JX, Samocha KE, Pierce-Hoffman E, Zappala Z, O'Donnell-Luria AH, Minikel EV, Weisburd B, Lek M, Ware JS, Vittal C, Armean IM, Bergelson L, Cibulskis K, Connolly KM, Covarrubias M, Donnelly S, Ferriera S, Gabriel S, Gentry J, Gupta N, Jeandet T, Kaplan D, Llanwarne C, Munshi R, Novod S, Petrillo N, Roazen D, Ruano-Rubio V, Saltzman A, Schleicher M, Soto J, Tibbetts K, Tolonen C, Wade G, Talkowski ME; Genome Aggregation Database Consortium, Neale BM, Daly MJ, MacArthur DG. The mutational constraint spectrum quantified from variation in 141,456 humans. *Nature* 2020; **581**: 434-443 [PMID: 32461654 DOI: 10.1038/s41586-020-2308-7]

18 **Larsen Haidle J**, MacFarland SP, Howe JR. Juvenile Polyposis Syndrome. In: Adam MP, Mirzaa GM, Pagon RA, Wallace SE, Bean LJH, Gripp KW, Amemiya A, editors. GeneReviews®. Seattle (WA): University of Washington, Seattle, 1993–2023

19 **van Leerdam ME**, Roos VH, van Hooft JE, Dekker E, Jover R, Kaminski MF, Latchford A, Neumann H, Pellisé M, Saurin JC, Tanis PJ, Wagner A, Balaguer F, Ricciardiello L. Endoscopic management of polyposis syndromes: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy* 2019; **51**: 877-895 [PMID: 31342472 DOI: 10.1055/a-0965-0605]

World Journal of Gastrointestinal Endoscopy

Submit a Manuscript: https://www.f6publishing.com

World J Gastrointest Endosc 2023 October 16; 15(10): 629-633

DOI: 10.4253/wjge.v15.i10.629

ISSN 1948-5190 (online)

CASE REPORT

Gallbladder plication as a rare complication of endoscopic sleeve gastroplasty: A case report

Cesar D Quiroz Guadarrama, Luis Andres Saenz Romero, Eric Misael Saucedo Moreno, Martín E Rojano Rodríguez

Specialty type: Gastroenterology and hepatology

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): B
Grade C (Good): C
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Cesaretti M, Italy; Correia de Sa T, Portugal

Received: July 4, 2023
Peer-review started: July 4, 2023
First decision: August 16, 2023
Revised: August 30, 2023
Accepted: September 7, 2023
Article in press: September 7, 2023
Published online: October 16, 2023

Cesar D Quiroz Guadarrama, Luis Andres Saenz Romero, Eric Misael Saucedo Moreno, Martín E Rojano Rodríguez, Obesity Clinic and Bariatric Surgery, Dr. Manuel Gea González General Hospital, México 14080, Mexico

Corresponding author: Eric Misael Saucedo Moreno, MCh, MMed, Associate Specialist, Obesity Clinic and Bariatric Surgery, Dr. Manuel Gea González General Hospital, Tlalpan 14080, Mexico, Mexico. eric.saucedo.m@gmail.com

Abstract

BACKGROUND

Endoscopic sleeve gastroplasty (ESG) is a minimally invasive procedure used in the treatment of obesity, with a complication rate of less than 2% of cases. There have been only two reported cases worldwide of gallbladder injuries as a major complication of ESG.

CASE SUMMARY

We present the case of a 34-year-old patient who developed a complication after ESG. The patient experienced epigastric and right hypochondrium pain 12 h after the procedure, and a positive Murphy's sign was identified on physical examination. Laboratory results showed a leukocyte count of 17 × 10^3/μL, and computed tomography indicated the presence of free fluid in the pelvic cavity and perihepatic recesses as well as a possible suture in the wall of the Hartmann's pouch toward the anterior surface of the stomach. A diagnostic laparoscopy was performed, revealing plication of the Hartmann's pouch wall to the anterior stomach wall. Laparoscopic cholecystectomy and lavage were carried out. The patient had a stable recovery and was discharged 72 h after surgery, tolerating oral intake.

CONCLUSION

Gallbladder plication should be suspected if signs and symptoms consistent with acute cholecystitis occur after ESG.

Key Words: Gastroplasty; Bariatric surgery; Complication; Endoscopy; Case report

Core Tip: Only two cases have been reported worldwide of gallbladder plication as a major complication of endoscopic sleeve gastrectomy. We present the case of a 34-year-old patient who experienced right hypochondrium pain after endoscopic sleeve gastrectomy with a positive Murphy's sign. Laboratory and imaging studies revealed acute cholecystitis findings and a possible gallbladder plication. Diagnostic laparoscopy confirmed plication of the Hartmann's pouch wall to the stomach. A cholecystectomy was performed with a favorable outcome.

Citation: Quiroz Guadarrama CD, Saenz Romero LA, Saucedo Moreno EM, Rojano Rodríguez ME. Gallbladder plication as a rare complication of endoscopic sleeve gastroplasty: A case report. *World J Gastrointest Endosc* 2023; 15(10): 629-633
URL: https://www.wjgnet.com/1948-5190/full/v15/i10/629.htm
DOI: https://dx.doi.org/10.4253/wjge.v15.i10.629

INTRODUCTION

Endoscopic sleeve gastroplasty (ESG) is performed using a suturing device placed at the tip of the endoscope, allowing for full-thickness suturing of the anterior, greater curvature, and posterior walls of the stomach[1-3]. While ESG is generally considered a safe procedure, some minor adverse effects have been observed, such as nausea, vomiting, and mild-to-moderate abdominal pain[4,5]. Only two cases have been reported worldwide of gallbladder plication as a major complication of ESG[6,7]. Due to its extreme rarity, there is no appropriate diagnostic and therapeutic protocol. Therefore, the relevance of this case report lies in identifying relevant clinical data in its presentation to develop a diagnostic strategy and potential treatments.

CASE PRESENTATION

Chief complaints

A 34-year-old female patient with a diagnosis of class I obesity (body mass index 30 kg/m^2) was admitted for scheduled ESG as primary treatment for obesity. ESG was performed under balanced general anesthesia, with the patient in the left lateral decubitus position. A suturing device (Apollo EndoSurgery, Austin, TX, United States) was used attached to a dual-channel therapeutic endoscope (Olympus 190; Olympus, Tokyo, Japan). The gastric cavity was insufflated with carbon dioxide, and continuous "U" sutures were placed from the gastric body-antrum junction to the fundus. Four sutures were used, each consisting of eight stitches, creating the anterior, greater curvature, and posterior walls of the stomach. Immediately after the procedure, the patient experienced two episodes of hematemesis and drowsiness.

History of present illness

The patient had a surgical history of two previous cesarean sections and a hysterectomy more than 5 years ago. She also had trauma to both pelvic limbs due to an accident, which required multiple reconstructive surgeries on her left foot. There had no history of bariatric surgery or previous placement of an intragastric balloon.

History of past illness

The patient denied any personal history of illness.

Personal and family history

The patient denied any family history of illness.

Physical examination

Immediately after the endoscopic procedure, the abdominal examination revealed a depressible abdomen without signs of peritoneal irritation, with present bowel sounds. Six hours after the procedure, the patient experienced epigastric pain and right hypochondrium pain with an intensity of 4/10 on the visual analog scale (VAS). She was able to tolerate a liquid diet, and her vital signs were stable with a blood pressure of 120/80 mmHg, heart rate of 89 beats per minute, and respiratory rate of 18 breaths per minute. However, 12 h after the procedure, the pain increased to an intensity of 8/10 on the VAS. During the physical examination, the abdomen was soft, and there was deep tenderness on palpation in the epigastrium and right hypochondrium, with a positive Murphy's sign.

Laboratory examinations

A complete blood count was requested, which showed white blood cell (WBC) count of 17.8 × 10^3/μL (normal range: 4.5-10.5 × 10^3/μL), with 91.9% (normal range: 40.0%-63.6%) segmented neutrophils.

Imaging examinations

An abdominal computed tomography scan was performed, revealing the presence of free fluid in the pelvic cavity at the

level of the posterior sac and perihepatic recesses on the right anterior segments. Postsurgical changes in the stomach were also observed, and an image suggestive of a possible suture in the gallbladder wall was noted (Figure 1).

FINAL DIAGNOSIS

Gallbladder plication following ESG.

TREATMENT

After evaluating the results, a diagnostic laparoscopy with intraoperative panendoscopy was performed. During the procedure, omental adhesions were identified in the gallbladder, a limited amount of free bile fluid was present, and a suture was found folding the gastric wall with the Hartmann's pouch of the gallbladder (Figure 2). Abdominal cavity lavage was performed with 2 L of 0.9% saline solution, followed by a routine cholecystectomy with a critical view of safety according to Strasberg's criteria without removing the suture. Intraoperative endoscopy was performed to confirm the absence of leaks into the abdominal cavity. Finally, a closed drainage was placed, and the surgical procedure was concluded.

OUTCOME AND FOLLOW-UP

Prophylactic intravenous ceftriaxone (1 g) was administered. During the first 12 postoperative hours, nonsteroidal anti-inflammatory drugs (intravenous parecoxib 40 mg every 12 h) and intravenous paracetamol (1 g every 8 h) were administered, and the patient continued fasting. At 24 h after surgery, the patient had stable vital signs, abdominal pain with an intensity of 3/10 on the VAS, and no nausea or vomiting with present peristalsis. The drainage output was less than 5 mL of serohematic fluid. Clear liquids were initiated orally 24 h after the surgical procedure, and a follow-up complete blood count was requested, which showed a decrease in WBC count to 13.0 × 10^3/μL (normal range: 4.5-10.5 × 10^3/μL). At 72 postoperative hours, the patient advanced to a soft diet with good tolerance, the drainage was removed, and she was discharged to home. During the follow-up visit at 7 d, the patient's recovery was satisfactory, without pain, tolerating a regular diet, and continuing with post-ESG nutritional management. At 30 d after surgery, the patient had a weight loss of 12 kg without complications.

DISCUSSION

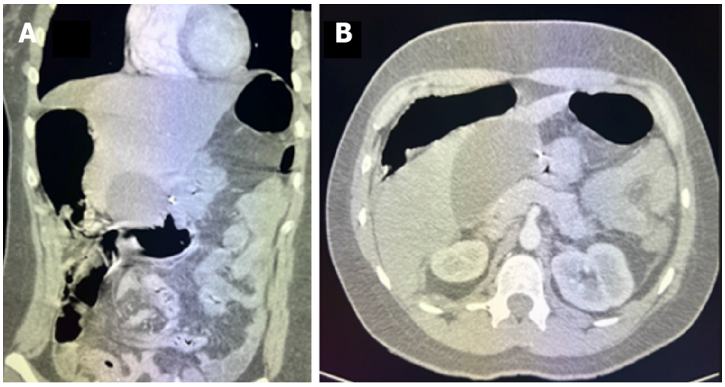
Obese patients with a high surgical risk or contraindication for abdominal surgery can benefit from minimally invasive endoscopic procedures[1-3,8]. The potential side effects during or after percutaneous endoscopic gastrostomy can be classified as minor or major. According to Alqahtani *et al*[4], minor symptoms affect 92.2% of patients and may include nausea, vomiting, and mild abdominal pain. Hedjoudje *et al*[9] conducted a meta-analysis of eight articles and concluded that major adverse events accounted for 2.2% of cases and were primarily related to transmural punctures that can occur during endoscopic suturing. These complications included unresponsive pain or nausea (1.08%), upper gastrointestinal bleeding (0.56%), leakage or perigastric collections (0.48%), pulmonary embolism (0.06%), and pneumoperitoneum (0.06%).

In the published medical literature, there are two cases of biliary tract plication following an ESG[6,7]. In our case, we were able to detect atypical symptoms in the patient's progression by considering the clinical suspicion and previous knowledge of this complication. Patients who experience epigastric pain radiating to the right hypochondrium and a positive Murphy's sign after an ESG should be considered as alarm signs.

After a detailed review of this case, several factors that could have contributed to this adverse event were identified. The patient's position during the procedure was left lateral decubitus, which could have caused the gallbladder to come into contact with the gastric antrum. It is suspected that the suture was initiated closer to the antrum than the gastric body, resulting in the plication of the gallbladder.

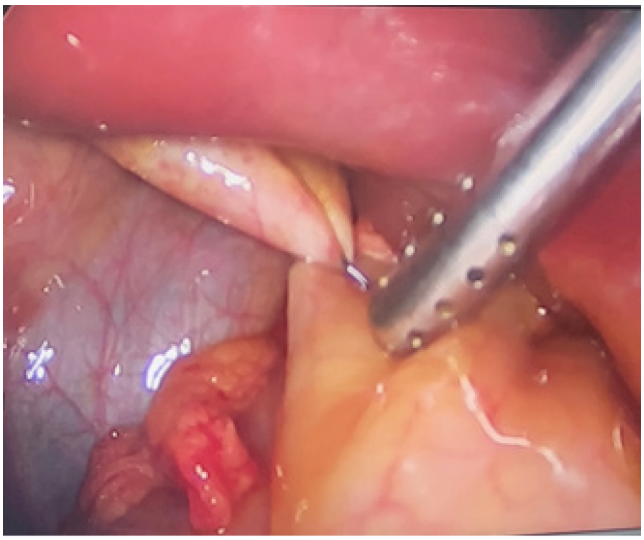
It is important to note that there is currently no standardized diagnostic protocol to detect complications following an ESG. However, in cases like the one described in this report where atypical symptoms and elevated leukocyte levels are present, a suggestive computed tomography scan showing biliary tract suture and a high clinical suspicion may be sufficient for a timely diagnosis.

Similarly, there is no standardized therapeutic approach defined for this complication. A surgical approach was chosen for our case upon consideration of the findings from computed tomography (which although inconclusive suggested the presence of free fluid in the abdominal cavity) as well as the possibility of suture in the biliary tract and the patient's elevated levels of leukocytes. Ultimately, this decision was based on the recommendations of the diagnostic laparoscopy guideline, which indicates its primary application following an initial diagnostic evaluation in patients with unexplained acute abdominal pain (of less than 7 d) or as an alternative to observation in cases of nonspecific abdominal pain[10].



DOI: 10.4253/wjge.v15.i10.629 **Copyright** ©The Author(s) 2023.

Figure 1 Computed tomography revealed a possible suture in the wall of the gallbladder fundus. A: Sagittal view; B: Axial view.



DOI: 10.4253/wjge.v15.i10.629 **Copyright** ©The Author(s) 2023.

Figure 2 Suture folding the gastric wall with the Hartmann's pouch of the gallbladder in laparoscopic cholecystectomy.

It is important to note that this intervention has been shown to be safe in appropriately selected patients[10]. In this context, we believe that the best treatment option is to perform a diagnostic laparoscopy, which provides diagnostic accuracy and consequently results in earlier diagnoses, shorter hospital stays, and a reduction in morbidity.

CONCLUSION

In summary, although there are no standardized diagnostic protocols or treatments for biliary tract plication following ESG, we recommend a multidisciplinary approach to diagnosis. Its presence should be suspected based on signs and symptoms consistent with acute cholecystitis, suggestive findings on computed tomography indicating plication or inflammation of the gallbladder, and laboratory results showing leukocytosis. Based on our experience, we recommend that the appropriate treatment includes a diagnostic laparoscopy followed by conventional cholecystectomy.

FOOTNOTES

Author contributions: Quiroz Guadarrama CD and Rojano Rodríguez ME conceived and designed the case report and performed the endoscopic and surgical procedures; Saenz-Romero LS collected all the data and recorded the imaging results related to the case; Saucedo Moreno EM performed analysis and interpretation of the data, drafted the report and reviewed the important concepts presented therein; All authors have read and approved the final manuscript.

Informed consent statement: We obtained the patient's written informed consent to disclose this case. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name will not be

published and due efforts will be made to conceal her identity.

Conflict-of-interest statement: All the authors declare having no conflicts of interest.

CARE Checklist (2016) statement: The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

Country/Territory of origin: Mexico

ORCID number: Cesar D Quiroz Guadarrama 0009-0000-4036-5141; Luis Andres Saenz Romero 0009-0002-8444-2086; Eric Misael Saucedo Moreno 0000-0002-1427-098X; Martín E Rojano Rodríguez 0000-0002-2218-3907.

S-Editor: Liu JH
L-Editor: A
P-Editor: Liu JH

REFERENCES

1 **Alqahtani AR**, Elahmedi M, Aldarwish A, Abdurabu HY, Alqahtani S. Endoscopic gastroplasty *vs* laparoscopic sleeve gastrectomy: a noninferiority propensity score-matched comparative study. *Gastrointest Endosc* 2022; **96**: 44-50 [PMID: 35248571 DOI: 10.1016/j.gie.2022.02.050]

2 **Nduma BN**, Mofor KA, Tatang JT, Ekhator C, Ambe S, Fonkem E. Endoscopic Gastric Sleeve: A Review of Literature. *Cureus* 2023; **15**: e36353 [PMID: 37082499 DOI: 10.7759/cureus.36353]

3 **Singh S**, Hourneaux de Moura DT, Khan A, Bilal M, Ryan MB, Thompson CC. Safety and efficacy of endoscopic sleeve gastroplasty worldwide for treatment of obesity: a systematic review and meta-analysis. *Surg Obes Relat Dis* 2020; **16**: 340-351 [PMID: 31932205 DOI: 10.1016/j.soard.2019.11.012]

4 **Alqahtani A**, Al-Darwish A, Mahmoud AE, Alqahtani YA, Elahmedi M. Short-term outcomes of endoscopic sleeve gastroplasty in 1000 consecutive patients. *Gastrointest Endosc* 2019; **89**: 1132-1138 [PMID: 30578757 DOI: 10.1016/j.gie.2018.12.012]

5 **Matteo MV**, Bove V, Pontecorvi V, De Siena M, Ciasca G, Papi M, Giannetti G, Carlino G, Raffaelli M, Costamagna G, Boškoski I. Outcomes of Endoscopic Sleeve Gastroplasty in the Elder Population. *Obes Surg* 2022; **32**: 3390-3397 [PMID: 35918595 DOI: 10.1007/s11695-022-06232-4]

6 **Lopez-Nava G**, Asokkumar R, Ielpo B, Bautista I, Vicente E. Biliary peritonitis after endoscopic sutured gastroplasty for morbid obesity (with video). *Gastrointest Endosc* 2019; **90**: 686-688 [PMID: 31375266 DOI: 10.1016/j.gie.2019.06.002]

7 **de Siqueira Neto J**, de Moura DTH, Ribeiro IB, Barrichello SA, Harthorn KE, Thompson CC. Gallbladder perforation due to endoscopic sleeve gastroplasty: A case report and review of literature. *World J Gastrointest Endosc* 2020; **12**: 111-118 [PMID: 32218890 DOI: 10.4253/wjge.v12.i3.111]

8 **Lopez-Nava G**, Asokkumar R, Bautista-Castaño I, Laster J, Negi A, Fook-Chong S, Nebreda Duran J, Espinett Coll E, Gebelli JP, Garcia Ruiz de Gordejuela A. Endoscopic sleeve gastroplasty, laparoscopic sleeve gastrectomy, and laparoscopic greater curve plication: do they differ at 2 years? *Endoscopy* 2021; **53**: 235-243 [PMID: 32698234 DOI: 10.1055/a-1224-7231]

9 **Hedjoudje A**, Abu Dayyeh BK, Cheskin LJ, Adam A, Neto MG, Badurdeen D, Morales JG, Sartoretto A, Nava GL, Vargas E, Sui Z, Fayad L, Farha J, Khashab MA, Kalloo AN, Alqahtani AR, Thompson CC, Kumbhari V. Efficacy and Safety of Endoscopic Sleeve Gastroplasty: A Systematic Review and Meta-Analysis. *Clin Gastroenterol Hepatol* 2020; **18**: 1043-1053.e4 [PMID: 31442601 DOI: 10.1016/j.cgh.2019.08.022]

10 **Hori Y**; SAGES Guidelines Committee. Diagnostic laparoscopy guidelines: This guideline was prepared by the SAGES Guidelines Committee and reviewed and approved by the Board of Governors of the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES), November 2007. *Surg Endosc* 2008; **22**: 1353-1383 [PMID: 18389320 DOI: 10.1007/s00464-008-9759-5]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: bpgoffice@wjgnet.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com