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Minimally invasive endoscopic repair of rectovaginal fistula

Zeng YX et al. Minimally invasive endoscopic repair of RVF

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Abstract

BACKGROUND

Surgical techniques for repair of rectovaginal fistula (RVF) have been continually developed, but the ideal procedure remains unclear. Endoscopic repair is a novel and

minimally invasive technique for RVF repair with increasing reporting.

AIM

To review the current applications and preliminary outcomes of this technique for RVF

repair, aiming to give surgeons an alternative in clinical practice.

METHODS

Available articles were searched according to the search strategy. And the sample size, fistula etiology, fistula type, endoscopic repair approaches, operative time and hospital stay, follow-up period, complication and life quality assessment were selected for

recording and further analysis.

RESULTS

A total of 11 articles were eventually identified, involving 71 patients with RVFs who

had undergone endoscopic repair. The principal causes of RVFs were surgery (n = 51,

71.8%), followed by obstetrics (n = 7, 9.8%), inflammatory bowel disease (n = 5, 7.0%), congenital (n = 3, 4.2%), trauma (n = 2, 2.8%), radiation (n = 1, 1.4%), and in two patients, the cause was unclear. Most fistulas were in a mid or low position. Several endoscopic repair methods were included, namely transanal endoscopic microsurgery, endoscopic clipping, and endoscopic stenting. Most patients underwent > 1-year follow-up, and the success rate was 40%-93%, and all cases reported successful closure. Few complications were mentioned, while postoperative quality of life assessment was only mentioned in one study.

CONCLUSION

In conclusion, endoscopic repair of RVF is novel, minimally invasive and promising with acceptable preliminary effectiveness. Given its unique advantages, endoscopic repair can be an alternative technique for surgeons.

Key Words: Endoscopic repair; Minimal-invasive technique; Rectovaginal fistula

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Core Tip: The current status of minimally invasive endoscopic repair for rectovaginal fistulas (RVFs) was reviewed. This is the first review to explore the current application status and evaluate the preliminary outcomes. Endoscopic repair is recommended as a novel and promising technique for RVF and warrants consideration by surgeons. The disappointing quality of published studies on surgical treatment of RVF is discussed, along with the possible role of endoscopic repair in improving the situation.

1 INTRODUCTION

Rectovaginal fistula (RVF), a type of chronic gastrointestinal fistula, refers to an abnormal epithelialized-lined connection between the rectum and the vagina, presenting with symptoms including uncontrollable passage of gas and/or fecal discharge from the vagina^[1]. Even though it is benign, the distressing and persistent symptoms interfere with daily activities and sexual life, and have a long-term potential detrimental impact on psychological health^[2,3]. Obstetric trauma is the primary etiological factor for RVF, but it can also be acquired from local abscess, pelvic floor or rectal surgery, trauma, or radiotherapy^[3-5]. Chronic inflammatory bowel disease (most commonly Crohn's disease) is the second most common etiology with rates varying between 6% and 23%^[6]. It is reported that RVF occurs in up to 10% of women diagnosed with Crohn's disease^[7,8]. Congenital RVF is rare, usually coexists with anal malformation, and can be treated by anal reconstruction at a young age^[9].

Standard classification of RVF will benefit to the choice of treatment approach and the comparison of treatment outcomes between studies, and help develop an algorithm for repair. However, there is no generally accepted classification of RVF. Currently, the classification of "simple/complex" or "low/middle/high" according to location, size, and etiology of RVF is most used^[10,11]. With the development of diagnostic and therapeutic techniques, the imaging results, endoscopic exploration and gradually defined local anatomical structure will promote a classification consensus^[12,13]. The anatomical features are always the principle of classification, which makes it necessary to achieve a more detailed and precise anatomical recognition^[14].

Various medical and surgical treatments have been applied for RVF, but treatment is still a challenge for doctors due to the high recurrence rate. Nonoperative methods are recommended for the treatment of fresh and slight symptomatic fistula. Surgical repair is essential, once it occurs and persists^[15]. There is still no standard surgical repair technique worldwide for RVF and no evidence can suggest one surgical technique over another since the release of the procedural guidelines in Europe.

Multiple surgical repair techniques, including fistulectomy, advancement flap, muscle transposition, closure with biomaterials, endoscopic repair and transabdominal approaches^[16], have been gradually reported in the literature. Fistulectomy is not technically demanding, whose main step is to remove the fistula tract, together with the surrounding scarred and sclerotic tissue. It may fail due to incomplete removal and excessive tissue tension of tissue suture for large excision, and is therefore, mostly used to repair small and simple RVFs[17,18]. Advancement flaps are performed by raising either the rectal mucosa (transrectal) or vaginal mucosa (transvaginal) to cover the fistula tract. Transrectal advancement flap is more commonly adopted compared to the transvaginal approach, and the repair is performed from the high pressure of the rectum side, and has an actual success rate of 50%-70% [1A]. Even though some studies have recommended transrectal advancement flap as the first-line treatment for low RVF, it is not as effective as expected if the periorificial tissue is chronically inflamed, or when the fistula is large in diameter and causes anal stenosis[19]. Reconstruction by Martius flap, gracilis muscle flap or bulbocavernosus muscle transposition can be used to introduce healthy vascularized tissues, which has achieved a certain effect for recurrent, Crohn's-disease-related and radiation-related RVF, with reported overall success rates ranging from 25% to 100% [20,21]. However, given the aggressive incision, tissue damage, prolonged hospital stay and protective stoma diversion routinely required, this technique is demanding and not easily accepted by patients[22,23]. Biomaterials and endoscopic repair are novel and less invasive techniques and constant attempts have been made to apply them for RVF repair. However, given the limited number of publications available, there are currently no relevant recommendations. Transabdominal approaches are recommended for high RVF resulting from complications of colorectal anastomosis, and laparoscopic repair has been frequently adopted[15,24]. In clinical practice, protective stoma diversion is generally applied for the treatment of RVF, whereas absence of any reliable efficacy assessment for RVF makes it remain controversial. Theoretically, diversion stoma may help control the symptoms by fecal diversion and support healing of the fistula and surgical success^[25]. Corte et al^[26]

claimed that a temporary diversion stoma could significantly improve the success rate of repair. However, Lambertz *et al*^[27] found no connection between diversion stoma creation and rate of recurrence, which was supported by other authors^[28,29]. Some studies have shown that radiation- and Chron's-disease-related RVFs are indications for diversion stoma^[30,31], and stating that once the diversion stoma is made, large invasion, distressing conditions and potential complications can occur^[32]. Although the techniques for RVF repair have been developing, the etiology, classification, surrounding tissue condition, prior treatment procedures and the surgeon's preference are always the basis for determining the approach. In addition, individualized, precise, and less-invasive surgical techniques for RVFs repair are gradually being recommended^[13,33].

All the surgical interventions performed via an endoscope or in the endoscopy unit can be classified as endoscopic repair, which is a novel and minimally invasive surgical technique for RVF. Several endoscopic repair approaches have been applied and reported for RVF surgical treatment. Transanal endoscopic microsurgery (TEMS) is an endoscopic technique performed entirely through the anus and rectum, which was originally developed in the 1980s to treat lower rectal adenomas^[34] (Figure 1). Vávra et al^[35] reported the first case of RVF treatment using TEMS in 2006, which is one of the most reported endoscopic approaches for RVF. Several minimally invasive endoscopic approaches such as the through-the-scope clip (TTSC), over-the-scope clip proctology system (OTSC) and endoscopic stenting have successively proven their role in RVF repair. After more than a decade of development, endoscopic repair for RVF has been continuously advanced and more advantages have been unveiled. Endoscopic repair for RVF is novel but limited by the information available. Therefore, a review of studies on minimally invasive endoscopic repair for RVF was carried out to assess the preliminary outcomes and introduce several endoscopic approaches for RVF surgical repair to surgeons, thereby contributing to developing a more individualized, precise, and less-invasive treatment plan appropriate for each patient.

MATERIALS AND METHODS

A search was performed to identify the existing literature available in PubMed and EMBASE databases in December 2021, without timeframe limitations (Figure 2). The following keywords, including "rectovaginal fistula," "rectovaginal," "fistula," "endoscope", "endoscopic," and "endoscopy", were used for searching. Given that there were only around 184 articles available, every single article was reviewed at the beginning. Exclusion criteria included irrelevancy, not English language, guidelines, or reviews. Articles published by the same author were found a duplication in the inclusion of patients, and the study with the longest follow-up was included. Three independent reviewers extracted and summarized data from the included articles and conducted qualitative assessment in accordance with the Oxford Centre for Evidence-Based Medicine 2011 Level of evidence [36]. All disagreements were settled by consensus. In addition, we conducted a research using Reference Citation Analysis (https://www.referencecitationanalysis.com/) and cited the relevant references.

RESULTS

A total of 11 articles were eventually identified according to the search strategy. Data were extracted by the reviewers and eventually reported using summary statistics, as shown in Table 1. The limited number of available articles and the low evidence of all studies made the primary outcome not sufficiently satisfactory. Besides, there were not enough eligible articles to perform a meta-analysis. In terms of the type of study, case reports seemed to be preferred for this novel technique, and the number of patients in each retrospective study was limited. The etiology was classified as: related to surgery (n = 51) such as rectal surgery, pelvic surgery and the colorectal anastomosis, *etc.*, with 22 patients undergoing rectal surgery with a history of radiotherapy; and directly caused by radiotherapy (n = 1), inflammatory bowel diseases (n = 5) including Crohn's disease and ulcerative colitis; congenital (n = 3), obstetric injury (n = 7), trauma (n = 2), with the etiology unclear in two patients. Most fistulas were situated in the middle or low. Most of the patients had undergone previous repairs, even on multiple occasions.

Fecal diversion was chosen as part of surgical treatment in some patients. Psychological components regarded as important as the success rate were rarely reported^[19,37], with improved sexual function after repair mentioned in only one paper.

Table 2 summarized the details and preliminary outcomes of endoscopic repair of RVFs. A total of 38 patients underwent the conventional surgical procedure with a transrectal endoscopic device, when the layered suture was closed for 24, and mucosal advancement flap was for 14 patients. Endoscopic clip was another commonly used approach for RVF repair, and 18 patients who were treated using this technique benefited from TTSC (n = 2) and OTSC (n = 16). One retrospective study reported endoscopic repair with placement of a self-expandable mental stent (n = 15). Several other endoscopic repair approaches for RVF such as endoscopic plugs, endoscopic injection and endoscopic-laparoscopic combined approach were noted, which were removed due to no complete references. Operating time and hospital stay were the desired outcomes, but not frequently reported. Most patients underwent > 1 year of follow-up. All case reports reported successful outcomes, but the success rates were different (40%-93%) in retrospective case series. More than half the studies reported no severe complications, and a few reported some minor postoperative complications, such as hematoma or abscess of rectovaginal septum (n = 2), moderate sphincter hypotonia (n = 1), pain (n = 5), minimal vaginal flatus (n = 1).

Minimally invasive endoscopic repair

TEMS: Minimally invasive techniques have been one of the major advancements in surgery in the last few decades, and are also one of the future trends. Such a technique has been almost routinely performed in colorectal resection irrespective of underlying diseases^[38]. With the development of surgical instruments, endoscopic surgery is considered a feasible and minimally invasive approach that can facilitate better exposure, direct visualization and precise operation, with an increasing number of surgeons choosing it^[39]. TEMS, as a platform for natural orifice transluminal endoscopic surgery, has developed into a well-established method of accurate resection of

specimens from the rectum under binocular vision after the initial application for rectal cancer, and has also been adopted as an operative intervention in an extended setting for RVF^[40]. After the first case of TEMS for RVF repair reported in 2006^[35], the first retrospective review with 13 patients who had undergone layered sutures via this repair technique was published in 2012, with a closure rate of 93%[41]. In the present review, more than half of patients (n = 38) underwent conventional surgical repair procedures with transanal endoscopic devices, with a success rate of 40%-93%. The latest study reported a closure rate of 82% of mid-low RVF TEMS with layered sutures and mucosal advancement flaps[42]. Another three cases all reported successful closure. The superior 3D exposure and direct vision were the greatest advantages of TEMS. Under good visualization, comprehensive procedures exploring the anatomical structural relationship could be provided preoperatively and intraoperatively. The conventional invasive procedure could be performed more accurately with TEMS equipment, and ensure complete removal of the surrounding scarred or granulomatous tissues, but without significant loss of normal tissue. Therefore, there was a greater certainty of adequate blood supply to the tissue overlaps and/or flaps owing to the fresh tissue with the healthy margins^[42]. In addition, the smaller tissue defect and good control of suture tightness enable free-tension repair^[43], and make up for the shortcomings of conventional local repair that cannot completely remove surrounding tissue and is subject to insufficient blood supply and prompt healing. Using a natural endoluminal approach with endoscopy, precise operation and visualization can greatly reduce the invasiveness of conventional surgery with less intraoperative bleeding, shorter operating time and hospital stay, and fewer postoperative complications.

Endoscopic clipping: Endoscopic clipping is another technology using endoclips to completely close gastrointestinal leaks and fistulas, initially applied for iatrogenic gastric perforation in 1993^[44]. John *et al* ^[45] reported the first successful closure of an RVF with TTSCs, which was also applied for repair of refractory RVF^[33]; Ortiz-Moyano *et al* ^[46] described a combined approach using TTSCs and tissue adhesive that improved

the rate of technical success in the endoscopic clips treatment of RVFs, since clips not only worked in opposing the margins, but acted as a scaffold for the glue. OTSCs for the gastrointestinal tract had greater force and a consistently high mean rate of procedural success of 80%-100%, and a durable clinical success rate of 57%-100%, and was preferred over TTSCs for closure of gastrointestinal fistulas[47]. Regarding colon perforation, small perforations (< 10 mm) could be successfully closed with TTSCs, whereas larger perforations could be successfully closed with OTSCs [48]. The first RVF closure using the OTSC proctology system was performed by Prosst et al^[49] in 2015. One prospective study in 2019^[50] presented the first evaluation of the therapeutic effects and safety of the application of OTSCs in complex RVFs, with a success rate of 43.7%, which was as high as that for gastrointestinal fistulas and convincing for complicated ones. Endoscopic clipping is a minimally invasive technique that involves transrectal placement of endoclips for RVF closure to avoid tissue incision, sphincter damage and intraoperative bleeding^[49]. It is considered suitable for small fistulas, and is even recommended to repair high-level fistulas^[45,48]. Given limited data and obtained evidence, the role of endoscopic clips in RVF repair remains to be further investigated.

Endoscopic stenting: Endoscopic stenting involves placement of a self-expandable mental stent into the gastrointestinal tract to treat the defects, especially anastomotic leaks or perforation of the upper gastrointestinal tract^[51]. Endoscopic placement of the self-expandable mental stent to treat RVFs after colorectal resection for cancer was a useful alternative to divert colostomy for the palliation of malignant rectal obstruction^[52]. The team presented the two series outcomes with a success rate of 83% (5 of 6 patients)^[53] and 80% (12 of 15 patients)^[54], and the fistula size decreased significantly in all remaining patients, indicating that endoscopic placement of self-expandable metal stents may be a valid adjunctive treatment of RVF after colorectal resection for cancer. However, the favorable results may have been due to the low number of patients and selection bias. In the selected cases, the endoscopic placement of the self-expandable metal stent for RVF repair showed that the endoscopic stenting

allowed a fast and proper closure of the fistula in a minimally invasive endoscopic way, with minor discomfort for patients and early discharge. A clear indication and results are still required for further in-depth study.

DISCUSSION

Surgical outcomes of RVF repair are mostly measured by the rates of closure and reoperation^[37]. The successful closure rates for RVF surgical repair vary in the literature^[55]. A similar variation in success rate (20%-93%) was found in this study using different etiologies and endoscopic approaches. We acknowledge that the varying rate of successful closure, limited number of publications available on this novel technique, and the low quality of included studies were limitations of the present review. In addition, the indications for endoscopic repair for RVF are not clear due to the lack of high-quality clinical studies. From a review of the included literature, endoscopic repair for RVF seems to be more commonly used in the treatment of low- and mid-level fistulas. However, it is also used for high-level fistulas with small openings, because transabdominal surgery is an invasive approach for small fistulas; therefore, endoscopic repair is considered a viable minimally invasive approach[48]. Moreover, endoscopic repair is a promising option for primary repair of RVF, and can be recommended for treatment of recurrent fistulas as well^[50]. Regarding endoscopic repair is performed locally, it is not suitable for refractory RVFs with large openings and excessive tissue defects. Nevertheless, the minimally invasive endoscopic approach for RVF repair is a promising choice, and more surgical methods could be developed based on the endoscopic technique. As the research progresses, more indications should be unveiled as well.

A 2014 systematic review claimed that the reason for difficulties in formulating a conclusion about the best surgical technique for RVF repair was the disappointing quality of existing literature surrounding different surgical techniques and outcomes for RVF repair^[16]. Such a result not only persisted in the present review, but also in some related to single surgical approaches^[8,20]. On the one hand, the limited number of

samples and the heterogeneity of etiology and local conditions made it hard to design large studies. RVF is a benign and chronic disease without a high incidence, but subject to variable and complex causes. There is no doubt that compared to the sample iatrogenic etiologies, IBDs-or radiation-related RVF would make difference in the local condition and the selection of surgical techniques. Therefore, retrospective studies were reviewed carefully to ensure the study sample size and homogeneity. With the continuous advancement of endoscopic techniques, different surgical procedures can be applied and standardized, which may improve the homogeneity of the surgical devices and contribute to designing large studies. On the other hand, in terms of the precise anatomical relationship of the fistula defect and the surrounding tissue, the lack of consensus on classification of RVFs makes it difficult to compare different surgical techniques. It is therefore proposed that further revisions are needed to guide the choice of newly developed treatment approaches^[19]. Additionally, some authors claimed that a precise preoperative anatomical relationship assessment allowed better classification of fistulas and comparisons among different techniques^[14]. It is believed that diagnostic imaging and endoscopic exploration could play a role in clarifying and developing anatomical relationship standards.

CONCLUSION

Endoscopic repair for RVFs is novel, effective and promising. A precise operation under good visualization through a natural lumen can reduce the invasiveness of conventional procedures. Some endoscopic surgical modes such as clipping and stenting mentioned in this review could even close the fistula without incision, less intraoperative bleeding, fewer complications, and shorter operating time and hospital stay. Surgeons could clarify the anatomical relationship of the fistula and surrounding tissue by endoscopic preoperative exploration and provide patients with a more appropriate treatment approach. However, endoscopic surgical repair for RVFs is technically demanding with a long learning curve and requires sufficient professional experience. Therefore, it is advocated to be performed by professional colorectal surgeons in highly specialized

centers. Besides, larger high-quality studies and longer follow-up studies are necessary to unveil the clear indication and advantages of this novel minimally invasive endoscopic technique for RVF repair.

ARTICLE HIGHLIGHTS

Research background

Rectovaginal fistula (RVF) is abnormal connections between the rectum and vagina. Surgical repair is essential, once it occurs and persists. Surgical techniques for repair of rectovaginal fistula have been continually developed, but the ideal procedure remains unclear. Endoscopic repair is a novel and minimally invasive technique for RVF repair with increasing reporting.

Research motivation

To review the current literature of endoscopic repair of RVF and highlight the novel and minimally invasive technique for RVF repair to surgeons.

Research objectives

To evaluate the preliminary outcomes of this technique for RVF repair and analyze the indication and technical superiority.

Research methods

We searched PubMed and EMBASE databases for available studies. Data were extracted and qualitative assessment was conducted.

Research results

The endoscopic repair of RVF is in constant development, including several available approaches. The preliminary effectiveness of endoscopic technique for RVF repair is acceptable.

Research conclusions

Endoscopic repair for RVF is novel, effective and promising with acceptable preliminary effectiveness. In this manuscript, we have provided a detailed review of literatures, summarized its indications and unique technical advantages and made suggestions for its application and future development.

Research perspectives

Endoscopic repair for RVF is effective and safe according to preliminary outcomes. It is a promising technique for the treatment of rectovaginal fistulas and provides a minimally invasive technique selection for surgeons to treat rectovaginal fistulas.

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- Kevin R Kniery. "Operative considerations for rectovaginal fistulas", World Journal of Gastrointestinal Surgery, 2015

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- Ming-Jin Huang, Dao-Xiong Ye, Yu Lin, Xing-Rong Lu, Hui-Ming Lin, Pan Chi, Ying Huang. "A nomogram for predicting rectovaginal fistula after low anterior resection for rectal cancer", Surgery Today, 2020 $_{\text{Crossref}}$

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- A. Lambertz, B. Lüken, T.F. Ulmer, G. Böhm, U.P. Neumann, C.D. Klink, C.J. Krones. "Influence of diversion stoma on surgical outcome and recurrence rates in patients with rectovaginal fistula A retrospective cohort study", International Journal of Surgery, 2016 $_{\text{Crossref}}$
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 - Li Xiao, Linlin Li, Guangyu Chen, Yong Zhang, Quanli Gao. "The lymphocyte-to-monocyte ratio could predict the efficacy of PD-1 inhibitors in patients with advanced cancer", Translational Cancer Research
 - M. Trompetto, A. Realis Luc, E. Novelli, R. Tutino, G. 8 words <1% Clerico, G. Gallo. "Use of the Martius advancement flap for low rectovaginal fistulas", Colorectal Disease, 2019 Crossref
 - Timo Weiland, Marion Fehlker, Thomas Gottwald, Marc O. Schurr. "Performance of the OTSC System in the endoscopic closure of iatrogenic gastrointestinal perforations: a systematic review", Surgical Endoscopy, 2013 Crossref

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