

## Current treatment of rectovaginal fistula in Crohn's disease

Yan-Fei Zhu, Guo-Qing Tao, Ning Zhou, Chen Xiang

Yan-Fei Zhu, Guo-Qing Tao, Ning Zhou, Chen Xiang, Department of General Surgery, Wuxi People's Hospital of Nanjing Medical University, No. 299, Qingyang Road, Wuxi 214023, Jiangsu Province, China

**Author contributions:** Zhu YF and Tao GQ designed the research; Zhu YF wrote the paper; Zhou N and Xiang C searched the references and analyzed them.

**Correspondence to:** Yan-Fei Zhu, MD, Department of General Surgery, Wuxi People's Hospital of Nanjing Medical University, No. 299, Qingyang Road, Wuxi 214023, Jiangsu Province, China. zhuyanfei\_2002@163.com

Telephone: +86-510-85350091 Fax: +86-510-82828435

Received: September 22, 2010 Revised: December 1, 2010

Accepted: December 8, 2010

Published online: February 28, 2011

### Abstract

Rectovaginal fistula (RVF) continues to be the most difficult perianal manifestation of Crohn's disease to treat. This devastating and disabling complication has a significant impact on patients' quality of life and presents unique management challenges. Current therapeutic approaches include many medical therapeutics and surgical treatments with a wide range of success rates reported. However, current evidence is lacking to support any recommendation. The choice of repair depends on various patient and disease factors and basic surgical tenets. In this article, we review the current options to consider in the treatment of Crohn's-related RVF, and try to evaluate their effects on fistulae closure and quality of life.

© 2011 Baishideng. All rights reserved.

**Key words:** Rectovaginal fistula; Crohn's disease; Advancement flap; Treatment; Relapse

**Peer reviewers:** Paola De Nardi, MD, Department of Surgery, Scientific Institute San Raffaele Hospital, Via Olgettina 60, Milan, 20132, Italy; Ronald S Chamberlain, MD, MPA, Chairman and Surgeon-in-Chief, Professor of Surgery, UMDNJ, Saint Barnabas Medical Center, 94 Old Short Hills Road, Livingston, NJ 07945, United States

Zhu YF, Tao GQ, Zhou N, Xiang C. Current treatment of rectovaginal fistula in Crohn's disease. *World J Gastroenterol* 2011; 17(8): 963-967 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v17/i8/963.htm> DOI: <http://dx.doi.org/10.3748/wjg.v17.i8.963>

### INTRODUCTION

Crohn's disease (CD) is a chronic inflammatory disorder with a variable clinical course that may occur anywhere in the alimentary tract, characterized by a tendency to form fistulas with adjacent structures. In addition, CD is the second most common cause of rectovaginal fistula (RVF) after obstetrical trauma. In general, the cumulative incidence of all perianal fistulas in CD is 50% after the age of 20, and up to 9% of these are RVFs. The incidence of Crohn's RVF is thought to be proportionate to the frequency and severity of large-bowel inflammation<sup>[1,2]</sup>. Although representing less than 10% of anal fistulas, RVF may cause significant clinical distress and social embarrassment. Common symptoms include dyspareunia, perianal pain, vaginal irritation, and poor hygiene leading to recurrent genitourinary infections<sup>[3]</sup>.

Accurate assessment is essential for planning management. The treatment of fistulas is based on the severity of symptoms, the anatomic location, the number and complexity of tracts and the presence of stricturing intestinal disease. Treatment options range from observation to medical therapeutics to the need for surgical intervention. Various surgical options have been suggested for RVF repair with a wide range of success rates, such as direct repair, fistulotomy, fibrin glue instillation, endorectal or vaginal advancement flap, abdominal procedures with colorectal or coloanal anastomosis, and epiploplasty. However, none has been universally accepted as the procedure of choice. The recurrence rates ranged from 25% to 50%<sup>[2-4]</sup>. In this article, we review the current options to consider in the treatment of Crohn's-related RVF and their effects on quality of life.

## TREATMENT CHOICE

The management involves an organized and detailed workup to accurately make the diagnosis and then implement the appropriate treatment. Only a combination of advanced imaging, physical examination, and clinical experience will afford the surgeon the opportunity to precisely identify the location and cause of this problem. There are no evidence-based randomized controlled trials for the appropriate management of RVFs. More focused studies targeting these patients with the use of combined medical and surgical therapy are necessary<sup>[1,4]</sup>.

### Medical treatment of Crohn's RVF

Treatment of RVF is mainly surgical. However, medical therapy does have a role in the treatment of Crohn's RVF. Over the years, attempts at healing Crohn's RVF by medical treatment have been met with failure. The principles of medical therapy have been aimed at the treatment of the underlying active disease and include the use of antibiotics, corticosteroids, immunosuppressives and infliximab.

Up to now, there have been no randomized, double-blind, placebo-controlled studies to support the use of antibiotics and corticosteroids in healing Crohn's RVF. These treatments are not favorable, with low rates of long-term symptomatic control and unacceptable high rates of recurrence. Besides, some local therapies, including warm sitz baths, antidiarrheal medications and so on, might provide minor relief from symptoms but are not curative measures<sup>[5]</sup>. More and more surgeons used them as adjuncts to surgical treatment of Crohn's RVF, despite the lack of clinical trials to establish their efficacy.

Antibiotics were found to display only short-term benefit for patients<sup>[6]</sup>. Some studies reported that more than 80% RVFs required complete fistula closure when cyclosporine was used in high doses intravenously. However, about one third of patients relapsed when therapy was switched from intravenous to oral. Furthermore, cyclosporine was associated with toxicity, especially nephrotoxicity in long-term therapy. Tacrolimus had a mechanism similar to cyclosporin, and preliminary reports showed fistula healing rates of up to 64% when combined with azathioprine, but further studies should be done to evaluate the efficacy<sup>[7]</sup>. The introduction of anti-tumor necrosis- $\alpha$  (TNF- $\alpha$ ) therapy has been a major advance in the treatment of fistulizing CD, and has completely altered treatment strategies for perianal disease<sup>[8,9]</sup>. About 25 women with Crohn's RVF were enrolled in the *post hoc* subset analysis of the ACCENT II (A CD Clinical trial Evaluating infliximab in a New long-term Treatment regimen in patients with fistulizing CD). After infusions of infliximab at weeks 0, 2, and 6, 60.7% and 44.8% of RVFs were closed at weeks 10 and 14. The duration of RVF closure was longer in the infliximab 5 mg/kg maintenance group than in the placebo group. They concluded that infliximab was effective in short-term closure of RVF, and maintenance treatment was more effective than placebo in prolonging RVF closure<sup>[10]</sup>. Parsi and his colleagues<sup>[11]</sup> studied the differences in response to infliximab among

patients with different types of Crohn's fistulas. The total closure rate for all external Crohn's fistulas was 78%, but the closure rate for Crohn's RVF was only 14% at 4 to 6 wk follow-up. Higashi *et al.*<sup>[12]</sup> reported that the frequency of neoplasia did not differ according to whether infliximab was used or not, but it was necessary to be careful in terms of long-term administration and to select patients in whom efficacy could be expected.

So far, medically induced fistula healing is rare with basic therapeutic approaches and is only short lived, with no challenging results of infliximab treatment for Crohn's RVF, which might due to a poorly vascularized rectovaginal septum<sup>[4,10]</sup>.

### Surgical treatment of Crohn's RVF

RVF in CD continue to be a challenging problem. A multistep approach has been recommended to treat patients with Crohn's-related RVF, in which medical treatment and drainage of local sepsis are the first initial steps to alleviate their discomfort before definitive surgical intervention is attempted<sup>[1,13,14]</sup>. Many reports believed that the presence of acute perianal sepsis needed to be separately addressed prior to any attempts to repair RVF. This may require surgical drainage accompanied by placement of a loose draining seton<sup>[15-17]</sup>. Subsequently, various surgical options have been suggested for RVF repair. Among them are direct repair, fistulotomy, fibrin glue instillation, endorectal or vaginal advancement flap, abdominal procedures with colorectal or coloanal anastomosis, and epiplooplasty<sup>[18-20]</sup>. There are no guidelines concerning optimal therapeutic approaches. Endoanal mobilization techniques such as the advancement flap technique were considered the therapy of choice for many years, but are now regarded ever more critically<sup>[21,22]</sup>. Surgical skill is very important and adherence to principles of hemostasis, gentle tissue handling and complete debridement of diseased tissue are imperative to success. The technique of repair will vary depending on the location of the fistula and extent of local and distant disease activity<sup>[23-25]</sup>.

Rectal advancement flap surgery is the most frequently used approach. A flap consisting of mucosa, submucosa, and some circular muscle fibers is elevated. The fistula tract is curetted and oversewn with synthetic absorbable suture. The distal end of the flap is then trimmed and sutured distal to the fistula opening. The repair is undertaken from the high-pressure side of a high low-pressure shunt, the primary source of the fistula is excised and a layer of intact healthy tissue is interposed. Rectal advancement flaps are best suited for Crohn's RVF when the fistula is low, the rectum is relatively spared, and there is no significant anal stenosis. However, this technique is contraindicated in patients with extensive ulceration or stricturing of the anal canal and transitional zone<sup>[26,27]</sup>. Alternative or additional surgical procedures include a rectal sleeve advancement flap and a vaginal advancement flap. An advancement sleeve flap may be a better option for those with circumferential anal canal or low rectal disease and a normal proximal rectum. This approach removes all diseased tissue in the anal canal and allows "normal"

rectal tissue to be sutured to the neodentate line<sup>[28]</sup>. Compared with a rectal flap, a vaginal flap is easier to mobilize. Sher *et al*<sup>[29]</sup> treated 14 patients using a transvaginal flap with excellent results, with complete healing in 13 patients. The authors believed that the success of this technique was to be attributed to the fact that they used healthy tissue from the vagina. Unfortunately no other authors have published their experience with this interesting technique and further conclusions are impossible to draw.

Tissue interposition methods were intended to interpose normal healthy tissue between suture lines and bring well-vascularized tissue into the area. The use of a gracilis muscle transplant is one of the various options and has been proposed for failed previous RVF repair. In Lefevre's study, for patients with CD, four of five (80%) presented no recurrent rectovaginal fistula after a median follow-up of 28 mo. They concluded that gracilis muscle transposition was a useful and effective method for the treatment of recurrent RVF, especially in patients with CD, providing a viable tissue flap between the rectum and the vagina. This procedure is associated with minor morbidity and a good success rate, especially in patients with CD<sup>[30]</sup>. However, despite healing, postoperative quality of life and sexual activity remained altered. Zmora *et al*<sup>[31]</sup> reported that the important technical features of the gracilis transposition procedure were fecal diversion, meticulous hemostasis, tension-free primary repair of the rectum after dissection and mobilization to a level of at least 3 cm above the fistula site, and a viable, tension-free, well-vascularized muscle pedicle. So they recommended it for Crohn's RVF, especially after failed previous repairs.

Advanced improvements in medical treatment and expert surgical management have decreased the need for proctectomy. However, recurrence has a major negative impact on the quality of life. The suboptimal quality of perianal tissues that are affected by CD is probably the origin of the failure to heal. As we know, adult stem cells extracted from certain tissues, such as adipose tissue, can differentiate into different tissues, such as muscle. García-Olmo *et al*<sup>[32]</sup> first reported a case of a young patient with CD who had a recurrent rectovaginal fistula that was treated by autologous stem cell transplantation with a lipoaspirate as the source of stem cells. Three months later the RVF still remained closed. The patient has not experienced vaginal flatus or fecal incontinence through her vagina. In any case, cell transplantation to overcome healing problems is a new surgical tool, and careful evaluation of this new modality might provide an opportunity to define a new era in the treatment of surgical challenges associated with healing disorders.

Failure, reoperations and recurrences of rectovaginal fistulas have a major impact on anal continence and quality of life. The technical feasibility of closing rectovaginal fistulas using new bioprosthesis such as Surgisis™ mesh has already been demonstrated. Surgisis™ is a biocompatible mesh generated from lyophilized porcine small intestinal submucosa, which allows host cells to replace and repair damage or defective tissue. The mesh is gradually replaced as the host cells rebuild and remodel

weakened tissue. Its sterile, acellular properties enable it to be used without the complication of rejection. There is a significant reduction in fibrosis during the healing process, because the mesh supports the patient's own connective tissue and smooth muscle growth<sup>[33]</sup>. Schwandner *et al*<sup>[34]</sup> reported that 21 patients with RVFs were performed with mesh procedures, the majority of them had Crohn's RVFs (nine). After a mean follow-up of 12 months, the success rates in relation to the presence of CD or not were 78% and 83% after primary mesh procedure separately. Besides, the success rates of RVF with only one prior attempt or at least two prior attempts were 88% and 62% respectively. Authors believed that this technique could potentially be an effective alternative or enrichment to "traditional" procedures such as advancement flap repair as the main procedure, or closure with muscle transposition. Further analysis is needed to assess the definitive role of this innovative technique in comparison to traditional surgical technique.

Complex RVFs are uncommon but difficult therapeutic problems. Local repair and flap advancement techniques have a high incidence of recurrence with poor functional outcomes. Transperineal repair with anal sphincter reconstruction, when indicated, and placement of a Martius flap result in improved rates of repair and better functional outcomes. A consecutive series of patients were retrospectively reviewed from a prospective database between 2002 and 2006 in McNevin's study<sup>[26]</sup>. They concluded that selected complex RVF can be reliably repaired with good functional outcomes using the Martius flap with anal sphincter reconstruction. Persistent or recurrent fecal incontinence and dyspareunia are common sequela of the underlying perineal injury and repair. However, the number of patients is small. Prospective randomized trials are lacking. Therefore, it remains questionable whether addition of a Martius flap improves outcome after rectovaginal fistula repair<sup>[27]</sup>.

The protective or definitive stoma (proximal fecal diversion) may be taken into consideration to control the symptoms before proceeding to a more definitive operation. Results are equivocal when a stoma is used in conjunction with repair of a Crohn's perianal fistula. Fecal diversion alone is not successful in healing the fistula despite an improvement of the anorectal Crohn's fistula. Stoma does not ensure success and is probably used in most complicated cases. Creating a stoma remains a controversial subject. Currently the decision to use a stoma is up to the surgeon's judgment at the time of operation with valuable results of physical and laboratory examinations.

## RESULTS OF VARIOUS TREATMENTS

A retrospective study reported by Athanasiadis<sup>[35]</sup> was concerned on a comparison of different techniques for recovery rates and functional results after repair for RVF in CD. The operations comprised 56 procedures performed in 37 women presenting with RVF. The follow-up period was 7.15 years. Several techniques were performed: transverse transperineal repair ( $n = 20$ ), endoanal direct closure multilayer without flap ( $n = 15$ ), anocutaneous

Table 1 Current reports for different repairs for rectovaginal fistulas with Crohn's disease

Authors	Patients/repairs	Procedure	Primary/overall healing (%)	Recurrence (%)	Follow-up (mo)
Joo <i>et al</i> <sup>[38]</sup> , 1998	20	RAF	-/75		17
Windsor <i>et al</i> <sup>[39]</sup> , 2000	13/21	Local repair	40/77	54	31
Athanasiadis <i>et al</i> <sup>[35]</sup> , 2007	37/56	various	51/73	30	85
	-/20	Transperineal repair	70		
	-/15	Direct closure	73		
	-/14	Anocutaneous flap	86		
	-/7	Advancement flap	29		
Ruffolo <i>et al</i> <sup>[36]</sup> , 2009	52/71	different	56/81	10	109
	-/36	RAF	56		
	-/23	VAF	57		

RAF: Rectal advancement flap; VAF: Vaginal advancement flap.

flap ( $n = 14$ ), and advancement mucosal or full-thickness flap ( $n = 7$ ). The success rates for each of the techniques in the above group were 70, 73, 86, and 29%, respectively. The transperineal repair led to decreased postoperative resting pressures. In the advancement flap technique, the resting and squeezing pressure decreased significantly. The risk of developing a suture line dehiscence leading to a persisting fistula was higher in the advancement flap procedure with 43%. Authors concluded that techniques with a low degree of tissue mobilization such as the direct closure and anocutaneous flap show higher success rates without significant postoperative changes in continence and manometric outcome. Impaired continence was observed only in the advancement flap group, resulting in significant changes in manometric values and recovery rates. The authors preferred to apply the direct multilayer closure technique without flap.

The research studied by Ruffolo evaluated the outcome of surgical repair of RVF in patients with Crohn's disease over a 14-year period and assessed the effect of therapy with antibody against TNF on healing<sup>[36]</sup>. The surgical techniques included ileocecal interposition, coloanal anastomosis, perineoproctotomy with sphincter repair, levatorplasty and closure of the fistula, rectal advancement flap and vaginal advancement flap. After initial drainage of anal sepsis and optimization of medical therapy, fistula closure was achieved in 81% of 52 patients. Overall, cumulative closure rates after the first, second, third and fourth attempts were 56, 75, 78 and 81%, respectively. The primary healing rate was similar in patients who received anti-TNF treatment before the first operation (12 of 18 patients) and those who did not (19 of 34), even though the former patients probably presented with more extensive and/or aggressive disease at some stage. This observation supports the notion that anti-TNF- $\alpha$  does not interfere with wound healing<sup>[37]</sup>. Furthermore, the current reports for different repairs for rectovaginal fistulas with CD are displayed in Table 1.

Crohn's-related rectovaginal fistulae have significant impact on quality of life including sexual function. El-Gazzaz<sup>[40]</sup> and coworkers obtained long-term follow-up of Crohn's-related rectovaginal fistulae to assess variables that influence surgical success and determine its effects on

quality of life and sexual function. Sixty-five women were identified at median follow-up of 44.6 months, of which 30 patients (46.2%) were successfully healed. Methods of repair included advancement flap ( $n = 47$ ), episio-proctotomy ( $n = 8$ ), colo-anal anastomosis ( $n = 7$ ), and fibrin glue or plug ( $n = 3$ ). Twenty-eight women (43.1%) were sexually active at follow-up, and of those, nine complained of dyspareunia, all within the unhealed group of patients. Sexual function and quality of life scores were comparable between healed and unhealed groups. They believed that healing increased when immunomodulators were used within three months before surgery. Smoking and steroids were predictors of repair failure. Regardless of successful healing, quality of life and sexual function were similar. Dyspareunia appears to be higher for women with unhealed fistulas<sup>[41]</sup>. Further research and multicenter studies should be performed.

## CONCLUSION

Crohn's-related RVF continues to be difficult to treat. Up to now, there has been no ideal treatment option suitable for all patients, and many techniques have been reported with a wide range of success. The reasonable combination of medical and surgical treatments should be recommended. The surgical management of RVF is complex and the best results come in conjunction with individualized care within specialist units. The technique should be carefully chosen depending on the anorectal morphology. Hopefully, ongoing studies will help produce a universally accepted algorithm that may enhance long-term outcomes. Further multicenter studies should be needed to evaluate the long-term effects of various approaches. Besides, the prognosis and the quality of life for affected women should not be ignored.

## REFERENCES

- 1 **Hannaway CD**, Hull TL. Current considerations in the management of rectovaginal fistula from Crohn's disease. *Colorectal Dis* 2008; **10**: 747-755; discussion 755-756
- 2 **Andreani SM**, Dang HH, Grondona P, Khan AZ, Edwards DP. Rectovaginal fistula in Crohn's disease. *Dis Colon Rectum* 2007; **50**: 2215-2222

- 3 **Casadesus D**, Villasana L, Sanchez IM, Diaz H, Chavez M, Diaz A. Treatment of rectovaginal fistula: a 5-year review. *Aust N Z J Obstet Gynaecol* 2006; **46**: 49-51
- 4 **Champagne BJ**, McGee MF. Rectovaginal fistula. *Surg Clin North Am* 2010; **90**: 69-82, Table of Contents
- 5 **Loungnarath R**, Dietz DW, Mutch MG, Birnbaum EH, Kodner IJ, Fleshman JW. Fibrin glue treatment of complex anal fistulas has low success rate. *Dis Colon Rectum* 2004; **47**: 432-436
- 6 **Dejaco C**, Harrer M, Waldhoer T, Miehsler W, Vogelsang H, Reinisch W. Antibiotics and azathioprine for the treatment of perianal fistulas in Crohn's disease. *Aliment Pharmacol Ther* 2003; **18**: 1113-1120
- 7 **Shafik A**. Treatment of rectovaginal fistulas. *Tech Coloproctol* 2003; **7**: 65-66; author reply 66
- 8 **Ricart E**, Panaccione R, Loftus EV, Tremaine WJ, Sandborn WJ. Infliximab for Crohn's disease in clinical practice at the Mayo Clinic: the first 100 patients. *Am J Gastroenterol* 2001; **96**: 722-729
- 9 **Ochsenkühn T**, Göke B, Sackmann M. Combining infliximab with 6-mercaptopurine/azathioprine for fistula therapy in Crohn's disease. *Am J Gastroenterol* 2002; **97**: 2022-2025
- 10 **Sands BE**, Blank MA, Patel K, van Deventer SJ. Long-term treatment of rectovaginal fistulas in Crohn's disease: response to infliximab in the ACCENT II Study. *Clin Gastroenterol Hepatol* 2004; **2**: 912-920
- 11 **Parsi MA**, Lashner BA, Achkar JP, Connor JT, Brzezinski A. Type of fistula determines response to infliximab in patients with fistulous Crohn's disease. *Am J Gastroenterol* 2004; **99**: 445-449
- 12 **Higashi D**, Futami K, Egawa Y, Hirano K, Tomiyasu T, Ishibashi Y, Simomura T, Nii K, Kuroki H, Maekawa T, Ono Y, Matsui T. Infliximab treatment for anal fistula in patients with Crohn's disease. *Anticancer Res* 2009; **29**: 927-933
- 13 **Taxonera C**, Schwartz DA, García-Olmo D. Emerging treatments for complex perianal fistula in Crohn's disease. *World J Gastroenterol* 2009; **15**: 4263-4272
- 14 **Agavov BA**, Dzhavadov EA, Abbasova GA. [Surgical treatment of rectovaginal fistulae]. *Khirurgiia (Mosk)* 2010; 44-46
- 15 **O'Connor L**, Champagne BJ, Ferguson MA, Orangio GR, Schertzer ME, Armstrong DN. Efficacy of anal fistula plug in closure of Crohn's anorectal fistulas. *Dis Colon Rectum* 2006; **49**: 1569-1573
- 16 **Pajares JA**, Hernández L, Menchén P, Menchén L. Duodenopancreatic fistula complicating upper gastrointestinal Crohn's disease: successful treatment with infliximab. *Am J Gastroenterol* 2009; **104**: 1863-1864
- 17 **Musaev KhN**. [Surgical treatment of rectovaginal fistulae]. *Khirurgiia (Mosk)* 2009; 55-58
- 18 **Willis S**, Rau M, Schumpelick V. [Surgical treatment of high anorectal and rectovaginal fistulas with the use of transanal endorectal advancement flaps]. *Chirurg* 2000; **71**: 836-840
- 19 **Giordano A**, della Corte M. Non-operative management of a rectovaginal fistula complicating stapled haemorrhoidectomy. *Int J Colorectal Dis* 2008; **23**: 727-728
- 20 **Li Destri G**, Scilletta B, Tomaselli TG, Zarbo G. Rectovaginal fistula: a new approach by stapled transanal rectal resection. *J Gastrointest Surg* 2008; **12**: 601-603
- 21 **Penninckx F**, Moneghini D, D'Hoore A, Wyndaele J, Coremans G, Rutgeerts P. Success and failure after repair of rectovaginal fistula in Crohn's disease: analysis of prognostic factors. *Colorectal Dis* 2001; **3**: 406-411
- 22 **Rahman MS**, Al-Suleiman SA, El-Yahia AR, Rahman J. Surgical treatment of rectovaginal fistula of obstetric origin: a review of 15 years' experience in a teaching hospital. *J Obstet Gynaecol* 2003; **23**: 607-610
- 23 **Schwartz DA**, Loftus EV Jr, Tremaine WJ, Panaccione R, Harmsen WS, Zinsmeister AR, Sandborn WJ. The natural history of fistulizing Crohn's disease in Olmsted County, Minnesota. *Gastroenterology* 2002; **122**: 875-880
- 24 **Thornton M**, Solomon MJ. Long-term indwelling seton for complex anal fistulas in Crohn's disease. *Dis Colon Rectum* 2005; **48**: 459-463
- 25 **Sonoda T**, Hull T, Piedmonte MR, Fazio VW. Outcomes of primary repair of anorectal and rectovaginal fistulas using the endorectal advancement flap. *Dis Colon Rectum* 2002; **45**: 1622-1628
- 26 **McNevin MS**, Lee PY, Bax TW. Martius flap: an adjunct for repair of complex, low rectovaginal fistula. *Am J Surg* 2007; **193**: 597-599; discussion 599
- 27 **Gosselink MP**, Oom DM, Zimmerman DD, Schouten RW. Martius flap: an adjunct for repair of complex, low rectovaginal fistula. *Am J Surg* 2009; **197**: 833-834
- 28 **Simmang CL**, Lacey SW, Huber PJ Jr. Rectal sleeve advancement: repair of rectovaginal fistula associated with anorectal stricture in Crohn's disease. *Dis Colon Rectum* 1998; **41**: 787-789
- 29 **Sher ME**, Bauer JJ, Gelernt I. Surgical repair of rectovaginal fistulas in patients with Crohn's disease: transvaginal approach. *Dis Colon Rectum* 1991; **34**: 641-648
- 30 **Lefèvre JH**, Bretagnol F, Maggiori L, Alves A, Ferron M, Panis Y. Operative results and quality of life after gracilis muscle transposition for recurrent rectovaginal fistula. *Dis Colon Rectum* 2009; **52**: 1290-1295
- 31 **Zmora O**, Tulchinsky H, Gur E, Goldman G, Klausner JM, Rabau M. Gracilis muscle transposition for fistulas between the rectum and urethra or vagina. *Dis Colon Rectum* 2006; **49**: 1316-1321
- 32 **García-Olmo D**, García-Arranz M, García LG, Cuellar ES, Blanco IF, Prianes LA, Montes JA, Pinto FL, Marcos DH, García-Sancho L. Autologous stem cell transplantation for treatment of rectovaginal fistula in perianal Crohn's disease: a new cell-based therapy. *Int J Colorectal Dis* 2003; **18**: 451-454
- 33 **Pye PK**, Dada T, Duthie G, Phillips K. Surgisistrade mark mesh: a novel approach to repair of a recurrent rectovaginal fistula. *Dis Colon Rectum* 2004; **47**: 1554-1556
- 34 **Schwandner O**, Fuerst A, Kunstreich K, Scherer R. Innovative technique for the closure of rectovaginal fistula using Surgisis mesh. *Tech Coloproctol* 2009; **13**: 135-140
- 35 **Athanasiadis S**, Yazigi R, Köhler A, Helmes C. Recovery rates and functional results after repair for rectovaginal fistula in Crohn's disease: a comparison of different techniques. *Int J Colorectal Dis* 2007; **22**: 1051-1060
- 36 **Ruffolo C**, Penninckx F, Van Assche G, Vermeire S, Rutgeerts P, Coremans G, D'Hoore A. Outcome of surgery for rectovaginal fistula due to Crohn's disease. *Br J Surg* 2009; **96**: 1190-1195
- 37 **Tougeron D**, Savoye G, Savoye-Collet C, Koning E, Michot F, Lerebours E. Predicting factors of fistula healing and clinical remission after infliximab-based combined therapy for perianal fistulizing Crohn's disease. *Dig Dis Sci* 2009; **54**: 1746-1752
- 38 **Joo JS**, Weiss EG, Nogueras JJ, Wexner SD. Endorectal advancement flap in perianal Crohn's disease. *Am Surg* 1998; **64**: 147-150
- 39 **Windsor ACJ**, Lunniss PJ, Khan UA, Rumbles S, Williams K, Northover JMA. Rectovaginal fistulae in Crohn's disease: a management paradox. *Int J Colorectal Dis* 2000; **2**: 154-158
- 40 **El-Gazzaz G**, Hull T, Mignanelli E, Hammel J, Gurland B, Zutshi M. Analysis of function and predictors of failure in women undergoing repair of Crohn's related rectovaginal fistula. *J Gastrointest Surg* 2010; **14**: 824-829
- 41 **Ellis CN**, Clark S. Effect of tobacco smoking on advancement flap repair of complex anal fistulas. *Dis Colon Rectum* 2007; **50**: 459-463

S- Editor Tian L L- Editor Cant MR E- Editor Lin YP