

## Retrospective Study

## Transanal endoscopic microsurgery as optimal option in treatment of rare rectal lesions: A single centre experience

Monica Ortenzi, Roberto Ghiselli, Maria Michela Cappelletti Trombettoni, Luca Cardinali, Mario Guerrieri

Monica Ortenzi, Roberto Ghiselli, Maria Michela Cappelletti Trombettoni, Luca Cardinali, Mario Guerrieri, Department of General Surgery, Università Politecnica delle Marche, 60126 Ancona, Italy

**Author contributions:** Ortenzi M and Ghiselli R designed the study; Ortenzi M, Cappelletti Trombettoni MM and Cardinali L contributed to acquisition of data and drafting the article; Guerrieri M approved the final version to be published.

**Institutional review board statement:** The study was reviewed and approved by the Ospedali Riuniti Institutional Review Board.

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

**Conflict-of-interest statement:** No financial support or incentive has been provided for this manuscript. All authors have no conflicts of interest or financial ties to disclose.

**Data sharing statement:** Technical appendix, original data, and statistical code of manuscript NO 26052 submitted to World Journal of Gastrointestinal Endoscopy are available from the corresponding author at [monica.ortenzi@gmail.com](mailto:monica.ortenzi@gmail.com). Participants gave informed consent for data sharing.

**Open-Access:** This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

**Manuscript source:** Invited manuscript

**Correspondence to:** Dr. Monica Ortenzi, Department of General Surgery, Università Politecnica delle Marche, Via Tronto 10/a, 60126 Ancona, Italy. [monica.ortenzi@gmail.com](mailto:monica.ortenzi@gmail.com)  
Telephone: +39-71-5963648  
Fax: +39-71-5963326

Received: March 28, 2016

Peer-review started: March 29, 2016

First decision: May 17, 2016

Revised: June 2, 2016

Accepted: July 11, 2016

Article in press: July 13, 2016

Published online: September 16, 2016

### Abstract

#### AIM

To analyze the outcomes of transanal endoscopic microsurgery (TEM) in the treatment of rare rectal condition like mesenchymal tumors, condylomas, endometriosis and melanoma.

#### METHODS

We retrospectively reviewed a twenty-three years database. Fifty-two patients were enrolled in this study. The lesions were considered suitable for TEM if they were within 20 cm from the anus. All of them underwent an accurate preoperative workup consisting in clinical examination, total colonoscopy with biopsies, endoscopic ultrasonography, and pelvic computerized tomography or pelvic magnetic resonance imaging. Operative time, intraoperative complications, rate of conversion, tumor size, postoperative morbidity, mortality, the length of hospital stay, local and distant recurrence were analyzed.

#### RESULTS

Among the 1328 patients treated by TEM in our department, the 52 patients with rectal abnormalities other than adenoma or adenocarcinoma represented 4.4%. There were 30 males (57.7%) and 22 females (42.3%). Mean age was 55 years (median = 60, range = 24-78). This series included 14 (26.9%) gastrointestinal stromal tumors, 21 neuroendocrine tumors (40.4%), 1 ganglioneuroma (1.9%), 2 solitary ulcers in the rectum (3.8%), 6 cases of rectal endometriosis (11.5%), 6

cases of rectal condylomatosis (11.5%) and 2 rectal melanomas (3.8%). Mean lesion diameter was 2.7 cm (median: 4, range: 0.4-8). Mean distance from the anal verge was 9.5 cm (median: 10, range: 4-15). One patient operated for rectal melanoma developed distant metastases and died two years after the operation. We experienced 2 local recurrences (3.8%) with an overall survival equal to 97.6% (95%CI: 95%-99%) at the end of follow-up and a disease free survival of 98% (95%CI: 96%-99%).

## CONCLUSION

We could conclude that TEM is an important therapeutic option for rectal rare conditions.

**Key words:** Transanal endoscopic microsurgery; Rare rectal conditions; Full-thickness excision; Minimally invasive surgery; Retrospective study

© The Author(s) 2016. Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** This paper is about the management of rare rectal lesions by transanal endoscopic microsurgery (TEM). The rarity of these conditions and the lack of big reports about this topic make this work important. We focused our attention on operative data and post-operative long-term outcomes. Our results suggested that TEM is a safe, minimally invasive procedure that can be adopted for the treatment of these conditions with excellent results.

Ortenzi M, Ghiselli R, Cappelletti Trombettoni MM, Cardinali L, Guerrieri M. Transanal endoscopic microsurgery as optimal option in treatment of rare rectal lesions: A single centre experience. *World J Gastrointest Endosc* 2016; 8(17): 623-627 Available from: URL: <http://www.wjgnet.com/1948-5190/full/v8/i17/623.htm> DOI: <http://dx.doi.org/10.4253/wjge.v8.i17.623>

## INTRODUCTION

Adenocarcinoma is the most frequent malignancy of the rectum, but the distal part of the bowel can host several other rare lesions which together represent an important part of rectal tumors<sup>[1]</sup>. This heterogeneous group comprehends mesenchymal tumors like gastrointestinal stromal tumors (GISTs), neuroendocrine tumors (NETs) and ganglioneuromas. Other abnormalities can involve the rectal wall, and surgery is the only curative option, as is also the case for condyloma, endometriosis and melanoma. The aim of this study was to analyze the results of transanal endoscopic microsurgery (TEM) in the treatment of these rare rectal conditions.

## MATERIALS AND METHODS

A retrospective accurate analysis of a twenty-two-year-old database built from 1992 to 2015 identified

52 patients eligible for the study. Indications for TEM were determined on the basis of the anatomical criteria assessed by rigid preoperative rectoscopy in order to locate the lesions and to measure its distance from the anal verge.

All patients were properly informed about the operation and give their consensus to surgery. The lesions were considered suitable for TEM if they were within 20 cm from the anus. Preoperative workup included clinical examination, total colonoscopy with biopsies, endoscopic ultrasonography, and pelvic computerized tomography or pelvic magnetic resonance imaging. Patients' characteristics such as age and gender were considered. All patients received similar pre-operative management with an oral intake of an osmotic solution the day before surgery and a short term intravenous antibiotics prophylaxis to provide coverage for the normal bowel flora, aerobic and anaerobic species.

Procedures were performed by the Wolf TEM equipment (Knittlingen, Germany) consisting of a rigid 12 or 20 cm long rectoscope, an endosurgical unit steadily controlling rectal endoluminal pressure, and curved instruments. In all cases, a full-thickness excision was performed, and the rectal defect was closed by a running suture secured with silver clips at the extremities.

The operative data examined included operative time, intraoperative complications and conversion to abdominal surgery. Tumor size was measured macroscopically and reported as the maximum diameter. Pathological examination included histopathological definition, degree of differentiation, macroscopical measurement, and the examination of radial margins of excision. A urinary catheter was placed in all the patients at the time of surgery, which was removed 24 h after the operation. In the post-operative period, we analyzed postoperative morbidity, mortality and the length of hospital stay. Long-term outcomes included local and distant recurrence. We considered as local recurrence any recurrence diagnosed endoscopically and confirmed by biopsy. Follow-up included digital examination, rigid rectoscopy and endorectal ultrasound every 6 mo for the first year from the time of operation and subsequently every year.

Quantitative variables are shown as the mean value with median and range in brackets. Recurrence-free survival was considered as a continuous variable. The probability of overall survival at the end of follow-up and the probability of disease-free survival were estimated using the Kaplan-Meier method. All analyses were performed using the R statistical package.

## RESULTS

Among the 1328 patients treated by TEM in our department, the 52 patients with rectal abnormalities other than adenoma or adenocarcinoma represented 4.4%. There were 30 males (57.7%) and 22 females (42.3%). Mean age was 55 years (median = 60, range = 24-78). We excised, by TEM, 14 (26.9%) GISTs, 21 NETs (40.4%), 1 ganglioneuroma (1.9%) and 2 solitary

**Table 1** Population characteristics *n* (%)

Variables	
Sex	
Male	30 (67.7)
Female	22 (42.3)
Neuroendocrine tumors	21 (40.4)
Gastrointestinal stromal tumors	14 (26.9)
Ganglioneuroma	1 (1.9)
Solitary ulcers	2 (3.8)
Endometriosis	6 (11.5)
Condylomas	6 (11.5)
Melanomas	2 (3.8)
Diameter (cm), [mean (median, range)]	2.7 (4, 0.4-8)

ulcers in the rectum (3.8%). We used TEM to treat 6 cases of rectal endometriosis (11.5%), 6 cases of rectal condilomatosis (11.5%) and 2 rectal melanomas (3.8%).

Preoperative symptoms ranged from rectal bleeding (9/52, 17.3%), urgency (3/52, 5.8%) and alteration in bowel habit (7/52, 13.5%). Thirty-two (61.5%) patients were asymptomatic and the lesions were discovered incidentally. Mean lesion diameter was 2.7 cm (median: 4, range: 0.4-8). Mean distance from the anal verge was 9.5 cm (median: 10, range: 4-15) (Table 1).

GISTs had a mean diameter of 1.4 cm (median = 1, range = 0.4-5). Two of them received neoadjuvant Imatinib resulting in reduction in tumor size. Six GISTs were defined as medium risk GISTs and 4 as high risk.

As for NETs, the mean lesion diameter was 2.7 cm (median = 2, range = 0.5-5). Except for one, all of them were G1 well differentiated NETs. There was only one ganglioneuroma which extended circumferentially on the rectal wall and had a diameter of 10 cm. The condyloma had a mean diameter of 2.7 cm (median: 3, range: 2-3). The 2 solitary ulcers had a diameter of 3 and 4 cm respectively and were completely excised.

Complete resection with disease-free margins was achieved in all the cases except for one case in which the pathologist was unable to assess the margin due to thermal damage. Mean operative time was 41 min (median: 45, range: 20-55). There was no conversion to abdominal surgery. We observed one intraoperative minor complication (1.9%) consisting in rectal bleeding controlled by TEM.

We observed a postoperative morbidity rate of 3.8% (2/50), consisting of one case of acute urinary retention and one case of mild incontinence to gas resolved within two months from the operation by means of physiotherapy. Mean hospital stay was 3 d (median: 4, range: 2-7).

All the patients completed the follow-up protocol, including clinical and instrumental assessment. Two patients (3.8%) died from unrelated causes. One patient with rectal NET showed local recurrence within a year after operation. One patient operated for rectal melanoma developed distant metastases and died two years after the operation (Table 2). We observed an overall survival equal to 97.6% (95%CI: 95%-99%) at the end of follow-up and a disease free survival of 98% (95%CI: 96%-99%) (Figure 1).

**Table 2** Operative and post-operative data *n* (%)

Variables	
Operative time-min [mean (median, range)]	41 (45, 20-55)
Intraoperative complications	1 (1.9)
Hospital stay (d) [mean (median, range)]	3 (4, 2-7)
Post-operative complications	2 (3.8)
Recurrence	1 (1.9)
Follow-up (yr) [mean (median, range)]	11 (13, 23-1)
Death at the end of follow-up	2 (3.8)

## DISCUSSION

Rectal lesions different from adenomas-carcinomas represent a small but important group in terms of oncological and functional implications. Surgery is the main choice in the treatment of these conditions, but debate regarding the best method for their management exists<sup>[1-3]</sup>. Their localization in the rectum may represent a therapeutical challenge. Most authors opt for anterior resection or even abdominal perineal resection, but traditional surgery may represent an overtreatment<sup>[1,2,4]</sup>.

NETs represent the largest group in our series. This kind of tumors are being diagnosed increasingly frequently, and current European Neuroendocrine Tumor Society guidelines recommend endoscopic resection for G1 rectal NET < 10 mm with a low risk of metastatic disease<sup>[5]</sup>. The current methods of endoscopic removal are polypectomy, endoscopic mucosal resection (EMR), endoscopic submucosal dissection (ESD) and TEM. Since complete surgical resection for a localized lesion was demonstrated as the only effective option, several studies have proved the superiority of TEM over the other endoscopic techniques in the treatment of rectal NET. EMR and ESD achieve a complete microscopic resection in 46.3% to 65.5% and in 75% to 82.6% of cases, respectively<sup>[6-11]</sup>. TEM allows us to achieve a 100% rate of free resection margins, as observed in other reports<sup>[9,10]</sup>. We did not observe cases of incomplete resection nor recurrence in our experience. Most tumors (80%) were ≤ 10 mm in diameter, and the risk of metastases has been estimated at less than 3% for rectal NETs within 1 cm in diameter<sup>[9]</sup>. In our series, all the lesions were G1 well-differentiated rectal NET without lymphovascular invasion except for one patient with a G3 poorly differentiated NET with lymphatic and vascular invasion, who relapsed within a year from operation and was treated by means of an abdominal perineal resection.

As for GISTs, according to Miettinen *et al.*<sup>[12]</sup>, the rectum is the third most common site of onset, comprising approximately 5%-10% of all GISTs. Neither radiation therapy nor chemotherapy has any proven efficacy as adjuvant therapy. Rectal GIST exhibits two specific features which may significantly affect surgical management: Metastases are extremely rare in loco-regional lymphnodes, and GISTs typically show a tendency to grow away from the intestinal lumen. These characteristics may make these tumors eligible for TEM<sup>[13-16]</sup>. In our series, all GISTs were completely resected by TEM. TEM excision is considered to be an interesting alternative

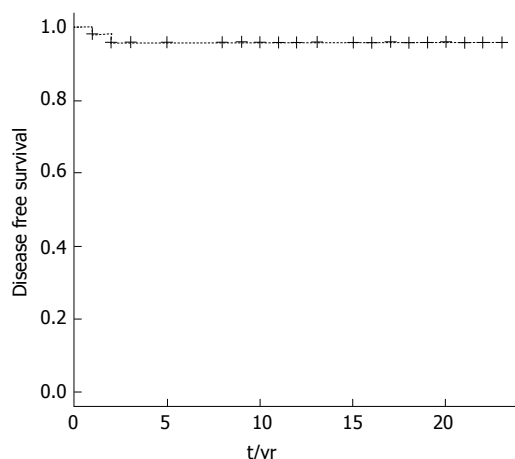


Figure 1 Disease free survival after transanal endoscopic microsurgery for rare rectal lesions.

for small GISTs located within the rectal wall, which are usually incidental findings during endoscopy. This approach, however, is considered not indicated for larger (> 5 cm) tumors growing away from the rectal lumen. In our series, only one GIST had a 5 cm diameter, but it was completely excised, and we did not observe recurrence.

Condyloma mainly affects the anorectal region, and rare reports have described condylomata involving the rectal wall which have often been incidentally discovered by endoscopy<sup>[17-19]</sup>.

Standard therapy such as laser, fulguration, freezing or microwaves can be difficult to apply inside the rectum<sup>[18]</sup>. Surgical resection by TEM can offer a good local disease control, and none of the patients treated by TEM experienced recurrence.

Rectum can also be the site of extrapelvic endometriosis<sup>[2,4,8,20]</sup>. Open or laparoscopic surgery is the primary mode of treatment in most of the infiltrating diseases. Surgical treatment is effective in relieving painful defecation, pelvic pain and dyspareunia<sup>[20]</sup>. We registered a positive resection margin in one patient affected by endometriosis, but no recurrence was observed in this case. Probably, the margin presented to the pathologist as elettro coagulated. Primary anorectal malignant melanoma is an extremely rare malignancy that is believed to arise from melanocytes in the mucosa around the anorectal junction. Surgery resection is the only curative option, but this malignancy is associated with poor prognosis<sup>[21,22]</sup>. We treated only two patients with rectal melanoma by TEM who were incidentally diagnosed during endoscopy. Both cases had an early stage of melanoma confirmed by the pathologist. Both patients received adjuvant chemotherapy. One of them developed local recurrence at 1 year from surgery and was treated with laparoscopic anterior resection.

TEM has demonstrated to be feasible in the treatment of different conditions different from adenomas and carcinomas which may affect the rectum. TEM allows us to reach lesions located up to 20 cm from the anal verge. The magnified tridimensional vision offered by TEM is

crucial to reach the complete rate of complete resection. The possibility to perform a full thickness excision of the rectal wall makes TEM appropriate for tumors like GISTs arising from submucosal layers.

In this series, we did not experience long term morbidity. We registered only one patient with mild gas incontinence which was resolved within two months from surgery by means of physiotherapy.

We could conclude that TEM is an important therapeutic option for rectal rare diseases. Other studies with more numerous series will be necessary to understand the real role of minimally invasive transanal techniques in the treatment of these lesions.

## COMMENTS

### Background

The rectum can be the site of origin of different lesion far more rare than adenocarcinoma but that have surgery as the only curative option. The full thickness excision reached by transanal endoscopic microsurgery (TEM) offers the possibility to achieve a complete resection with very low morbidity.

### Research frontiers

TEM has several advantages compared with traditional approach. It allows to perform a complete transanal full thickness excision of the lesions, with an accurate individuation of free margins due to a magnified stereoscopic view. The morbidity related to this approach is low compared to other surgical techniques.

### Innovations and breakthroughs

The exact role of TEM in the treatment of rare rectal lesions is hard to define mainly due to the lack of large series. The retrospective analysis of the authors' experience allowed them to built one of the largest series now available on this topic.

### Applications

This retrospective analysis of the authors' experience suggest TEM can be considered safe and feasible in the treatment of these lesions.

### Peer-review

This is a large retrospective analysis on the treatment of rare rectal lesions by TEM. The paper is overall well written. The results are well reported.

## REFERENCES

- 1 **Jakob J**, Mussi C, Ronellenfitch U, Wardelmann E, Negri T, Gronchi A, Hohenberger P. Gastrointestinal stromal tumor of the rectum: results of surgical and multimodality therapy in the era of imatinib. *Ann Surg Oncol* 2013; **20**: 586-592 [PMID: 22965573 DOI: 10.1245/s10434-012-2647-1]
- 2 **Roman H**, Tuech JJ, Resch B, Leroi AM, Marpeau L, Michot F. Letter re: "Complete surgery for low rectal endometriosis: long-term results of a 100-case prospective study". *Ann Surg* 2013; **257**: e18-e19 [PMID: 23665974 DOI: 10.1097/SLA.0b013e31828d6ff2]
- 3 **Caplin M**, Sundin A, Nillson O, Baum RP, Klose KJ, Kelestimir F, Plöckinger U, Papotti M, Salazar R, Pascher A. ENETS Consensus Guidelines for the management of patients with digestive neuroendocrine neoplasms: colorectal neuroendocrine neoplasms. *Neuroendocrinology* 2012; **95**: 88-97 [PMID: 22261972 DOI: 10.1159/000335594]
- 4 **Haggag H**, Solomayer E, Juhasz-Böss I. The treatment of rectal endometriosis and the role of laparoscopic surgery. *Curr Opin Obstet Gynecol* 2011; **23**: 278-282 [PMID: 21666468 DOI: 10.1097/GCO.0b013e328348a25b]
- 5 **Ramage JK**, De Herder WW, Delle Fave G, Ferolla P, Ferone D, Ito T, Ruszniewski P, Sundin A, Weber W, Zheng-Pei Z, Taal B, Pascher A. ENETS Consensus Guidelines Update for Colorectal



- Neuroendocrine Neoplasms. *Neuroendocrinology* 2016; **103**: 139-143 [PMID: 26730835 DOI: 10.1159/000443166]
- 6 **Jeon SM**, Lee JH, Hong SP, Kim TI, Kim WH, Cheon JH. Feasibility of salvage endoscopic mucosal resection by using a cap for remnant rectal carcinoids after primary EMR. *Gastrointest Endosc* 2011; **73**: 1009-1014 [PMID: 21316666 DOI: 10.1016/j.gie.2010.12.029]
  - 7 **Lee SH**, Park SJ, Kim HH, Ok KS, Kim JH, Jee SR, Seol SY, Kim BM. Retraction notice to "endoscopic resection for rectal carcinoid tumors: comparison of polypectomy and endoscopic submucosal resection with band ligation". *Clin Endosc* 2015; **48**: 87 [PMID: 25674848 DOI: 10.5946/ce.2015.48.1.87]
  - 8 **Sung HY**, Kim SW, Kang WK, Kim SY, Jung CK, Cho YK, Park JM, Lee IS, Choi MG, Chung IS. Long-term prognosis of an endoscopically treated rectal neuroendocrine tumor: 10-year experience in a single institution. *Eur J Gastroenterol Hepatol* 2012; **24**: 978-983 [PMID: 22647741 DOI: 10.1097/MEG.0b013e3283551e0b]
  - 9 **Jeon JH**, Cheung DY, Lee SJ, Kim HJ, Kim HK, Cho HJ, Lee IK, Kim JI, Park SH, Kim JK. Endoscopic resection yields reliable outcomes for small rectal neuroendocrine tumors. *Dig Endosc* 2014; **26**: 556-563 [PMID: 24447261 DOI: 10.1111/den.12232]
  - 10 **Chen WJ**, Wu N, Zhou JL, Lin GL, Qiu HZ. Full-thickness excision using transanal endoscopic microsurgery for treatment of rectal neuroendocrine tumors. *World J Gastroenterol* 2015; **21**: 9142-9149 [PMID: 26290641 DOI: 10.3748/wjg.v21.i30.9142]
  - 11 **Sekiguchi M**, Sekine S, Sakamoto T, Otake Y, Nakajima T, Matsuda T, Taniguchi H, Kushima R, Ohe Y, Saito Y. Excellent prognosis following endoscopic resection of patients with rectal neuroendocrine tumors despite the frequent presence of lymphovascular invasion. *J Gastroenterol* 2015; **50**: 1184-1189 [PMID: 25936647 DOI: 10.1007/s00535-015-1079-7]
  - 12 **Miettinen M**, Lasota J. Gastrointestinal stromal tumors: review on morphology, molecular pathology, prognosis, and differential diagnosis. *Arch Pathol Lab Med* 2006; **130**: 1466-1478 [PMID: 17090188]
  - 13 **Hassan I**, You YN, Dozois EJ, Shayyan R, Smyrk TC, Okuno SH, Donohue JH. Clinical, pathologic, and immunohistochemical characteristics of gastrointestinal stromal tumors of the colon and rectum: implications for surgical management and adjuvant therapies. *Dis Colon Rectum* 2006; **49**: 609-615 [PMID: 16552495 DOI: 10.1007/s10350-006-0503-8]
  - 14 **Khalifa AA**, Bong WL, Rao VK, Williams MJ. Leiomyosarcoma of the rectum. Report of a case and review of the literature. *Dis Colon Rectum* 1986; **29**: 427-432 [PMID: 3709322 DOI: 10.1007/BF02555068]
  - 15 **Changchien CR**, Wu MC, Tasi WS, Tang R, Chiang JM, Chen JS, Huang SF, Wang JY, Yeh CY. Evaluation of prognosis for malignant rectal gastrointestinal stromal tumor by clinical parameters and immunohistochemical staining. *Dis Colon Rectum* 2004; **47**: 1922-1929 [PMID: 15622586]
  - 16 **Helewa RM**, Rajaei AN, Raiche I, Williams L, Paquin-Gobeil M, Boushey RP, Moloo H. The implementation of a transanal endoscopic microsurgery programme: initial experience with surgical performance. *Colorectal Dis* 2016; Epub ahead of print [PMID: 26990716 DOI: 10.1111/codi.13333]
  - 17 **Musquer N**, Bossard C, Coron E. An uncommon combination of polyps. *Gastroenterology* 2014; **147**: e1-e2 [PMID: 25064549 DOI: 10.1053/j.gastro.2014.03.037]
  - 18 **Remorgida V**, Ferrero S, Fulcheri E, Ragni N, Martin DC. Bowel endometriosis: presentation, diagnosis, and treatment. *Obstet Gynecol Surv* 2007; **62**: 461-470 [PMID: 17572918]
  - 19 **Ye Y**, Sun XZ, Feng JS. Woman with rectal condyloma acuminatum: a case report. *Int J Clin Exp Med* 2015; **8**: 6365-6368 [PMID: 26131258]
  - 20 **Darwish B**, Roman H. Surgical treatment of deep infiltrating rectal endometriosis: in favor of less aggressive surgery. *Am J Obstet Gynecol* 2016; Epub ahead of print [PMID: 26851598 DOI: 10.1016/j.ajog.2016.01.189]
  - 21 **Matsuda A**, Miyashita M, Matsumoto S, Takahashi G, Matsutani T, Yamada T, Kishi T, Uchida E. Abdominoperineal resection provides better local control but equivalent overall survival to local excision of anorectal malignant melanoma: a systematic review. *Ann Surg* 2015; **261**: 670-677 [PMID: 25119122 DOI: 10.1097/SLA.0000000000000862]
  - 22 **Ballo MT**, Gershenwald JE, Zagars GK, Lee JE, Mansfield PF, Strom EA, Bedikian AY, Kim KB, Papadopoulos NE, Prieto VG, Ross MI. Sphincter-sparing local excision and adjuvant radiation for anal-rectal melanoma. *J Clin Oncol* 2002; **20**: 4555-4558 [PMID: 12454112]

**P- Reviewer:** McSorley ST, Samardzic S, Santoro GA, Sterpetti AV

**S- Editor:** Gong ZM **L- Editor:** A **E- Editor:** Li D





Published by **Baishideng Publishing Group Inc**

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)

Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>

<http://www.wjgnet.com>

