ISSN 1948-5190 (online)

World Journal of *Gastrointestinal Endoscopy*

World J Gastrointest Endosc 2015 September 10; 7(12): 1045-1082

Published by Baishideng Publishing Group Inc

WJGE World Journal of Gastrointestinal Endoscopy

A peer-reviewed, online, open-access journal of gastrointestinal endoscopy

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2014-2017

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World Journal of Gastrointestinal Endoscopy

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Biweekly Volume 7 Number 12 September 10, 2015

World Journal of Gastrointestinal Endoscopy
Volume 7 Number 12 September 10, 2015

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NAME OF JOURNAL
World Journal of Gastrointestinal Endoscopy

ISSN
ISSN 1948-5190 (online)

LAUNCH DATE
October 15, 2009

FREQUENCY
Biweekly

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

PUBLICATION DATE
September 10, 2015

World Journal of Gastrointestinal Endoscopy

Submit a Manuscript: http://www.wjgnet.com/esps/
Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
DOI: 10.4253/wjge.v7.i12.1045

World J Gastrointest Endosc 2015 September 10; 7(12): 1045-1054
ISSN 1948-5190 (online)

REVIEW

Laparoscopic surgery for rectal prolapse and pelvic floor disorders

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Author contributions: Rickert A and Kienle P designed the review, performed the literature search, interpreted the data, wrote the paper and finally approved the manuscript.

Conflict-of-interest statement: The authors have no conflicts of interest or financial ties to disclose.

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Received: April 28, 2015
Peer-review started: May 6, 2015
First decision: June 2, 2015
Revised: June 22, 2015
Accepted: August 25, 2015
Article in press: August 31, 2015
Published online: September 10, 2015

Abstract

Pelvic floor disorders are different dysfunctions of gynaecological, urinary or anorectal organs, which can present as incontinence, outlet-obstruction and organ prolapse or as a combination of these symptoms. Pelvic floor disorders affect a substantial amount of people, predominantly women. Transabdominal procedures play a major role in the treatment of these disorders. With the development of new techniques established open procedures are now increasingly performed laparoscopically. Operation techniques consist of various rectopexies with suture, staples or meshes eventually combined with sigmoid resection. The different approaches need to be measured by their operative and functional outcome and their recurrence rates. Although these operations are performed frequently a comparison and evaluation of the different methods is difficult, as most of the used outcome measures in the available studies have not been standardised and data from randomised studies comparing these outcome measures directly are lacking. Therefore evidence based guidelines do not exist. Currently the laparoscopic approach with ventral mesh rectopexy or resection rectopexy is the two most commonly used techniques. Observational and retrospective studies show good functional results, a low rate of complications and a low recurrence rate. As high quality evidence is missing, an individualized approach is recommend for every patient considering age, individual health status and the underlying morphological and functional disorders.

Key words: Resection rectopexy; Pelvic floor disorders; Rectal prolapse; Laparoscopy; Mesh rectopexy; Suture rectopexy

Core tip: Pelvic floor disorders are dysfunctions of the pelvic organs which affect a substantial amount of people, predominantly women. Operative treatment is often necessary and laparoscopic procedures play a major role. Many different techniques are used but their functional and operative outcome is hardly evaluated in randomised studies. In this review we summarize the present status of laparoscopic surgery for pelvic floor disorders. The different techniques are described,

compared and rated concerning their operative outcome, functional results and recurrence rates. Clinically important topics like management of complications and surgery in elderly people are highlighted.

Rickert A, Kienle P. Laparoscopic surgery for rectal prolapse and pelvic floor disorders. *World J Gastrointest Endosc* 2015; 7(12): 1045-1054 Available from: URL: http://www.wjgnet.com/1948-5190/full/v7/i12/1045.htm DOI: http://dx.doi.org/10.4253/wjge.v7.i12.1045

INTRODUCTION

The term pelvic floor disorders summarises different dysfunctions of gynaecological, urinary or anorectal organs. These dysfunctions can present as incontinence, outlet-obstruction and organ prolapse or as a combination of these symptoms. The underlying reasons for these problems can be functional or morphological. Rectocele, enterocele and rectal intussusception are the most frequently encountered morphological manifestations and are commonly associated with a descensus of the perineum. The judgement on to what extent these anatomic disorders are clinically relevant and account for the associated bowel dysfunctions (incontinence, constipation) is difficult, as they often occur in combination and are also frequently found in healthy people[1,2]. The prevalence in women is about 25% for at least one of the above morphological pelvic floor abnormalities, somewhat questioning the clinical implications of such diagnosis *per se*.

Complete rectal prolapse is defined as protrusion of all layers of the rectum through the anal canal, full thickness rectal prolapse (FRP). A protrusion of mucosa only is called mucosa prolapse (MP). The clinical differentiation between these two can be difficult.

A common classification divides three grades: Rectal prolapse Ⅰ°: inner (recto-rectal) intussusception of the rectum proximal of the anal canal; Rectal prolapse Ⅱ°: inner (recto-anal) intussusception into the anal canal; Rectal prolapse Ⅲ°: prolapse of the rectum beyond the anus (external prolapse).

The aetiology is unclear. Rectal prolapse is often associated with obesity, pregnancy, chronic constipation and other conditions that lead to increased abdominal pressure.

The most common anatomic varieties in patients with rectal prolapse are redundant sigmoid, diastases of the elevator ani, loss of the vertical position of the rectum and its sacral attachments and a deep cul-de-sac[3,4].

The pathological relevance of an internal prolapse is unclear. A rectal prolapse Ⅰ° is present in 20% to 50% of healthy individuals[2,5]. On the other hand a recent study on 86 patients with internal rectal prolapse found faecal incontinence in 55% and showed incomplete evacuation in 45% of patients[6]. The intussusceptions that are found in people without symptoms are more often only a MP, whereas patients with evacuation problems significantly more often have a full thickness prolapse[7].

The differentiation to anal prolapse which is a protrusion of anoderm is important as the latter prolapse is generally operated *via* a perineal approach.

A rectocele is a protrusion of the rectum into the vagina. An enterocele/sigmoidocele is a prolapse of the peritoneal sack between rectum and vagina with herniation of small bowel respectively sigmoid. The clinical relevance of these anatomical varieties is also unclear. It is thought that larger rectoceles can lead to outlet obstruction with incomplete emptying. Defecographies showed an incidence of up to 93% in healthy women. Enteroceles can be found in up to 20% of healthy woman[2,5].

A prospective evaluation of 100 patients with obstructive defecation syndrome (ODS) found a combination of rectocele and MP in 54% of patients[8]. Dvorkin *et al*[7] tried to define certain predictive symptoms in 896 patients with evacuation disorders. They used an evacuation proctography and found 125 patients with rectal intussusception, 100 patients with rectocele and 152 patients with both pathologies. Anal pain and sensation of prolapse were predictive for the subsequent finding of an isolated intussusception rather than a rectocele.

In a systematic review on laparoscopic ventral rectopexy (LVR) for ODS all patients had a rectocele, 90% had an intussusception and 51% had an enterocele[9].

OPERATION PROCEDURES

Multiple operations have been described for the therapy of pelvic floor disorders. In the following section techniques and results of operations as far as they are performed laparoscopically are explained and rated (Tables 1 and 2).

The aim of the operation generally is to correct the morphologic alteration and thereby treat the symptoms of the patient, *e.g.*, improve incontinence or constipation and incomplete emptying, depending on what major symptoms the patient is suffering from. This can be achieved by three ways: (1) fixation of the rectum (rectopexy); (2) resection or plication of redundant bowel; and (3) mobilisation of the rectum. Most operations combine the two principles of rectal mobilisation and rectopexy, some operations add bowel resection.

The approach can be transanal/perineal or transabdominal. Abdominal operations seem to result in lower recurrence rates, but there are no randomised controlled trials substantiating this[10,11]. Perineal procedures avoid laparotomy/laparoscopy and therefore may have a lower operative risk and morbidity. They may therefore be more suitable for older or high-risk

Table 1 Abdominal procedures for pelvic floor disorders

Type of procedure	Operation technique
Suture rectopexy (Sudeck)	Complete rectal mobilisation to level of levators Suture of rectum to presacral fasica
Anterior sling rectopexy (Ripstein)	Complete rectal mobilisation to level of levators circular wrapping of mesh around rectum and attachment to the promontory
Lateral mesh rectopexy (Orr-Loygue)	Anterior + posterior complete rectal mobilisation fixation by two lateral mesh strips to promontory
Ventral mesh rectopexy (D'Hoore)	Strictly anterior rectal dissection to level of levators Fixation of mesh strip on distal rectum and to promontory
Posterior mesh rectopexy (Wells)	Complete rectal mobilisation to level of levators Semicircular mesh around rectum posterior, fixation to promontory
Resection rectopexy (Frykman-Goldberg)	Complete rectal mobilisation to level of levators sigmoid resection and suture fixation of rectum to promontory
Rectal mobilisation without rectopexy	Complete rectal mobilisation to level of levators no fixation

Table 2 Outcome of laparoscopic procedures for pelvic floor disorders

	Minor compl.	Major compl.	Mortality	Conversion	Incontinence	Constipation	Recurrence
LSR	0%-16%	2%-11%	0%	0%-5%	48%-82% (+)	11% (-)-70% (+)	2%-20%
LMR	0%-5%	0%-3%	0%	0%-5%	76%-92% (+)	38% (-)-36% (+)	1.3%-6%
LVR	0%-36%	0%-5%	0%-0.4%	0%-7.4%	70%-90% (+)	60%-80% (+)	0%-14%
LRR	11%-21%	0%-4%	0%-0.8%	0%-6%	62%-94% (+)	53%-80% (+)	0%-11%

Data from studies that report data of laparoscopic rectopexy. Incontinence/constipation: Improvement (+), worsening (-); Minor compl.: Dindo Ⅰ-Ⅱ; Major compl.: Dindo Ⅲ-Ⅳ. LSR: Lap. suture rectopexy; LMR: Lap. mesh rectopexy (Wells, Orr-Loygue); LVR: Lap. ventral rectopexy; LRR: Lap. resection rectopexy.

patients with a relevant co-morbidity, although again there are no adequately powered RCTs to back these recommendations up.

Virtually all abdominal procedures that were originally described *via* laparotomy can also be performed laparoscopically. The laparoscopic management of rectal prolapse was first introduced in 1992 and consisted of a suture-less rectopexy with staples without bowel resection. In the meantime, besides the conventional laparoscopic approach, there are new reports of a robotic-assisted approach with the da-Vinci system[12,13]. The transabdominal operations differ mainly in the extent of rectal mobilisation, the method of rectal fixation and the additional sigmoid resection.

RECTOPEXY

The fixation of the rectum to the sacrum is supposed to restore the physiological position of the rectum and thereby also correct the descensus of the pelvic floor. The fixation can be achieved by simple stitching, stapling or by meshes.

SUTURE RECTOPEXY (SUDECK)

This method was first described by Sudeck in 1922. The operation includes a complete mobilisation of the rectum down to the level of the levators. The rectum is then attached to the promontory by suture or staples. The dorsal mobilisation induces fibrosis which helps to fixate and hold the rectum in place[14].

In the literature this technique was used mostly to treat full rectal-prolapse in some cases combined with outlet obstruction or occasionally for outlet obstruction alone. Morbidity rates of 0% to 16% and no mortality were reported[15-18]. Conversion rates were between 0% and 5%. Most reports showed an improvement of incontinence, while constipation was mostly unchanged or even slightly worsened. Recurrence rates were between 2% and 9%[19]. A study which performed a longer follow-up found a recurrence rate of 20% ten years after laparoscopic suture rectopexy[17].

RECTOPEXY WITH MESH OR GRAFT

A mesh or graft is used to achieve a broader fixation and induce more fibrosis. Used materials include fascia lata, synthetic meshes and bio-meshes[20]. The mesh can be placed anteriorly, posteriorly, laterally or around the rectum.

ANTERIOR MESH RECTOPEXY (RIPSTEIN SLING RECTOPEXY)

Ripstein[21] described this operative technique in 1952. After complete mobilisation of the rectum a graft constructed out of the fascia lata was wrapped around the rectum and sutured to the promontory. Later instead of a fascia lata graft, synthetic meshes are used.

There is only one case report on this procedure using a laparoscopic approach which found a good clinical outcome (no morbidity, no recurrence)[22].

LATERAL MESH RECTOPEXY (ORR-LOYGUE)

In this procedure the rectum is completely mobilised anteriorly and posteriorly. Two mesh strips are sutured laterally to the rectum on both sides. The mesh strips are then sutured under tension to the promontory[23].

Several studies examined this technique with a laparoscopic approach. Lechaux *et al*[24] performed 35 laparoscopic Orr-Loygue rectopexies. They reported a surgical morbidity of 5% and no mortality. Incontinence improved in 27% of patients, constipation improved in 19%, but worsened in 27%. The recurrence rate was 6% after a follow-up of 36 mo. A study on 73 patients with an Orr-Loygue procedure with limited lateral dissection found an improvement of incontinence in 90% and of constipation in 60% of patients[25].

POSTERIOR MESH RECTOPEXY (WELLS)

After a complete mobilisation of the rectum a mesh is placed around the posterior circumference of the rectum (2/3) and then fixed to the promontory. The ventral third of the rectal circumference is spared to avoid fibrosis and stenosis by shrinking of the mesh.

A prospective study examined the Wells' procedure in 77 patients with FRP. It observed no major post-operative complications. Incontinence improved in 89% of patients, constipation improved in 36%[26]. Recurrent prolapse occurred in one patient (1.3%). Older studies evaluating laparoscopic posterior mesh rectopexy found similar results, but with a worsening of constipation in 20%-30% of patients, which might be caused by injury of autonomic nerves during posterior dissection[27].

VENTRAL MESH RECTOPEXY (D'HOORE)

In 2004 D'Hoore *et al*[28] published the results of a novel, autonomic nerve-sparing rectopexy technique. The dissection in this operation is strictly ventral in the rectovaginal space down to the pelvic floor. A lateral or dorsal mobilisation is not performed. The rectum is attached to the sacrum by a mesh which is sutured to the anterior side of the rectum. The ventral dissection and position of the mesh has several advantages: (1) a supra-anal rectocele can be corrected; (2) the rectovaginal septum is reinforced which prevents an anterior recto-rectal intussusception which may be one of the relevant mechanisms to a full rectal prolapse; and (3) a colpopexy is performed. The avoidance of any lateral or posterior mobilisation preserves the autonomic nerves[29].

Although LVR is a comparably new method it was rapidly adopted and up to now, more than 30 retro- and prospective series have reported outcome and postoperative function. Two systematic reviews have summarized the data.

Indications for the procedures were intussusception as well as overt rectal prolapse, rectocele, ODS and vaginal vault prolapse.

The rate for minor complications was 0% to 36%, major complications were observed in 0% to 5%. Reported typical but infrequent complications were erosions of the bowel or the vagina caused by the mesh or a dislocation of the mesh in about 4% of patients. Two studies reported the rare event of a lumbosacral discitis at the site of the proximal mesh fixation in 3 patients[30,31].

The conversion rate ranged from 0% to 7.4%. In most cases the conversions had to be made due to pelvic or abdominal adhesions after prior surgery.

Recurrence rates in the literature range from 0% to 15%, with most studies reporting recurrences in less than 5% of patients after a follow-up of a minimum of two years.

The median hospital stay ranged from 1 to 7.1 d. One study showed that a same day discharge was possible in selected patients and that more than 90% of patients could be discharged the day after surgery with the same long term outcome[32].

Fifty percent to 93% of patients operated with LVR suffered from constipation pre-operatively, between 44% and 93% of patients had faecal incontinence. Bowel function improved significantly in all studies with improvement rates from 70% to 90% for incontinence and 60% to 80% for constipation. Seven percent to 27% complained of persisting constipation and 0% to 18% of persisting incontinence. A new onset of constipation was found in 2% to 7% of patients[9,28,33]. Sexual function also showed significant improvement postoperatively[34,35].

Despite the good results, the rapid adoption and distribution of this new method without any high level evidence has to be seen critically[36].

RESECTION RECTOPEXY (FRYKMAN-GOLDBERG)

A sigmoid resection is combined with a rectopexy, mostly a sutured rectopexy. The resection results in the following morphologic changes: (1) an area of fibrosis develops around the anastomosis and the sacrum which leads to a rectal fixation to the sacrum; and (2) the colon lies in a straighter course which avoids torsion and sigmoidocele[37].

Especially in patients with an elongated sigmoid and slow-transit constipation it is postulated that constipation improves through the resection of redundant colon. A recent study, however, could not confirm an improvement in abnormal colonic transit time in patients after resection rectopexy[38].

Furthermore it must be considered that a removal of a part of the colon can alter bowel function independently from the underlying pelvic floor disorder. A recent study reported impaired bowel function and quality of life after sigmoid resection for diverticulitis[39,40]. Resection

of the sigmoid and creation of an anastomosis can contribute to perioperative morbidity (leakage, stenosis, ureter lesion).

Indications for resection rectopexy in the available studies were intussusception, external rectal prolapse, rectocele and ODS.

In studies for laparoscopic resection rectopexy (LRR) a minor complication rate between 11% and 21% and a major complication rate between 0% and 4% were observed. Anastomotic leakages occurred very rarely (< 1%). Only an older study from 1998 reported a leakage rate of 3.3%[41]. A low mortality rate between 0% and 0.3% was observed.

The conversion rate for LRR ranges from 0% to 6%. The reasons for conversion were mainly adhesions[42-45].

The recurrence rates ranged from 0% to 11% after a follow-up of a minimum of 4 years. The median hospital stay ranged from 4 to 9.7 d.

LRR improved incontinence in 62% to 94% of patients and constipation in 53% to 80% of patients with rectal prolapse[44,45].

LRR was performed for ODS in one study. Sixty percent of patients showed a rectocele, 60% had a rectal prolapse Ⅰ°-Ⅲ° and 50% had sigmoidocele. In 40% of patients the incontinence and the constipation ceased, in further 40% the symptoms improved irrespective of the underlying morphologic pathology[46].

ROLE OF ABDOMINAL PROCEDURES AND LAPAROSCOPY

Concerning the large number of different operative methods and the poor evidence it does not surprise that evidence based guidelines for treatment do not exist for pelvic floor disorders.

A recent survey asked 391 surgeons over 50 countries for their preferred method for the treatment of rectal prolapse. It revealed that 60% of surgeons would treat healthy patients with an external prolapse with a laparoscopic abdominal procedure, 20% would chose an abdominal method *via* laparotomy and only 20% favoured a perineal approach. For internal prolapse still 40% of the surgeons preferred laparoscopy. While in Europe LVR is the most popular treatment for external prolapse, surgeons in North America favour LRR[47].

An expert consensus paper published in 2013 explicitly recommends a laparoscopic or robotic approach for ventral rectopexy[48].

LEARNING CURVE OF LAPAROSCOPIC RECTOPEXY

The learning curve for laparoscopic colorectal surgery has been found to be around 150 to 200 cases for achieving a constant level of proficiency[49,50]. This also seems to apply to laparoscopic rectopexy. One large single-surgeon series found a proficiency level of 54 patients for operation time and about 100 patients for clinical and functional outcome parameters even for an experienced colorectal surgeon[51]. This adds to the difficulties in evaluating different procedures, as in most studies the experience of the surgeon was not defined.

COMPARISON OF LAPAROSCOPIC AND OPEN PROCEDURES

Evidence from randomised studies that compared laparoscopic with open rectopexy is rare. A Cochrane systematic review from 2008 found that the laparoscopic approach resulted in fewer postoperative complications and a shorter hospital stay compared to the open approach. But these findings are based on only two randomised studies comprising altogether 60 patients. Both studies used a ventral mesh fixation without resection[52-54] (Table 3).

Postoperative major complications were only cardiorespiratory and occurred only in the group with an open operation. A faster recovery (return to solid diet) and a reduced requirement for morphine were found for the laparoscopic group, which altogether resulted in a shorter hospital stay. But no difference was found for functional parameters (incontinence, constipation, rectal capacity, anal squeeze pressure) and recurrence rates.

Two case controlled studies compared open and laparoscopic surgery for rectal prolapse. Kairaluoma *et al*[55] used different procedures in 106 patients (LRR, suture rectopexy, Wells rectopexy). A longer operation time (170 min *vs* 100.5 min) but a shorter hospital stay (5 d *vs* 7 d) was found for laparoscopy. Functional outcome, recurrence rates and complications did not differ between case- and control-group. Kariv *et al*[56] found similar results. In this study also different techniques were applied. One third of patients in each group had resection rectopexy respectively suture rectopexy respectively mesh rectopexy (predominantly Ripstein anterior rectopexy for open surgery, Well's procedure in laparoscopic surgery). Incontinence and constipation improved in all patients, with a significant higher improvement in the laparoscopic group (74% *vs* 54%). A likely explanation for this finding was the much more frequent use of the Ripstein procedure in the open surgery group where the circular anterior mesh placement can result in a stenosis which obviously in turn contributes to the occurrence of constipation[57]. For this reason a circular mesh placement is now considered obsolete by most authors.

de Hoog *et al*[58] compared open rectal prolapse surgery to a conventional laparoscopic and a robot-assisted approach in a prospective non-randomised setting. Half of the patients were operated with the Wells procedure, the other half with a ventral rectopexy. While the functional outcome (incontinence, constipation) improved significantly in all three groups, the recurrence rates during a 2-year follow-up were significantly increased in the robot-assisted (20%) and the conventional laparoscopic group (27%) *vs* 2% in

Table 3 Comparative rectopexy studies (open *vs* laparoscopic, different procedures)

Study	Procedure	Patients	Results
Sajid (2009)	LR	330	No difference in Mort, Morb, Inc, Cons, recurrence shorter hospital stay for LR
Meta-analysis (12 studies)	OR	358	Shorter operation times for OR
different procedures			
Caddedu (2012)	LR	192	No difference in Mort, Morb, Inc, Cons, recurrence
Meta-analysis (8 studies)	OR	275	
different procedures			
Senapeti (2013)	SR	38	No difference in morbidity, recurrence and functional outcome
Randomised	RR	40	
Forminje (2014)	LVR	40	More minor complications in LRR
Retrospective	LRR	28	No difference in major complications, recurrence and functional outcome
Sahoo (2014)	LPR	38	No differences in morbidity, recurrence and functional outcome
Retrospective	LSR	32	
Lechaux (2004)	LRR	13	Significant more patients with worsening of constipation in the LMR-group (26% *vs* 8%)
Prospective	LMR	35	No differences in morbidity and improvement of continence
Madbouly (2002)	LRR	12	No difference in complications and functional outcome
Prospective	LPR	12	

Data from studies that compare open *vs* laparoscopic rectopexies or studies that compare different procedures. Mort: Mortality; Morb: Morbidity; Inc: Faecal incontinence; Cons: Constipation; LR: Laparoscopic rectopexy; OR: Open rectopexy; SR: Suture rectopexy; RR: Resection rectopexy; LPR: Laparoscopic posterior mesh rectopexy; HS: Hospital stay; OT: Operation time.

the open group. However, there was an imbalance in patient distribution, with more young patients in the laparoscopic group. In these patients a vaginopexy was generally not performed, which proved to be a protective factor in regard to recurrence on multi-variate analysis.

In a recent meta-analysis, 12 comparative studies comprising 688 patients (330 with laparoscopic rectopexy) were analysed[59]. A drawback of this meta-analysis was that only one study was randomised and that several different procedures (resection, non-resection) were used even within studies. Nevertheless a significant shorter hospital stay was found for the laparoscopic group, while no differences between the open and laparoscopic approach were found for complication rates, postoperative functional outcome, recurrence rates and mortality. A meta-analysis from 2012 showed the same results[60].

As a conclusion: the laparoscopic approach for rectal prolapse is equivalent to the open approach in terms of functional and clinical outcome. The recurrences rates do not seem to differ, although single studies suggest higher recurrence rates after laparoscopic surgery. Advantages are a shorter hospital stay. It has to be remarked that the evidence is based on only two randomised and a few prospective and comparative case-controlled studies with significant heterogeneity in patient characteristics and in applied surgical procedures, making a relevant selection bias very probably.

COMPARISON OF DIFFERENT LAPAROSCOPIC PROCEDURES

Studies comparing the different operation techniques are rare. One randomised trial compared suture rectopexy (38 patients) with resection rectopexy (40 patients). After a median follow-up of 36 mo fewer recurrences were seen in patients with resection (13%) compared to patients with suture rectopexy (26%), but the difference was not statistically significant. Functional results were not different expect that the use of laxatives was more common at all time points in the suture rectopexy group. This suggests that resection has a positive effect on constipation[11].

Formijne Jonkers *et al*[45] compared 40 patients with LVR to 28 patients with LRR for full rectal prolapse in a retrospective cohort study. Patients with LRR suffered from significantly more complications (32% *vs* 7.5%), but these were mainly minor complications (wound infections, pneumonia), the rate of major complications was not different. Both groups showed a significant improvement in faecal incontinence (LVR 40% *vs* LRR 57%) and constipation (LVR 36% *vs* LRR 32%). In this study no recurrences were observed in a median follow-up period of 4 years.

Laparoscopic posterior rectopexy was compared to suture rectopexy retrospectively by Sahoo *et al*[61] in 70 patients. Suture rectopexy had a shorter operation time (100 min *vs* 120 min). The improvement of constipation (suture rectopexy 61% *vs* mesh rectopexy 47%) and incontinence (SR 90% *vs* MR 80%) was not different.

A comparison between LRR and LR without resection in 67 patients with FRP revealed that more patients with resection improved in incontinence while constipation improved similarly in both groups.

In a multi-centre randomised trial, Karas *et al*[62] evaluated, if a sole rectal mobilisation without rectopexy was equal to a posterior mesh rectopexy. Two hundred and forty-five patients were randomised. In case of constipation sigmoid resection was added. The degree of rectal mobilisation (posterior or 360°) was up to the surgeon's decision.

After a 5-year follow-up the recurrence rate in the group without rectopexy was significantly higher than in

the group with rectopexy (8.6% *vs* 1.5%, P = 0.003). This was despite the fact that sigmoid resection was significantly more often performed in the group without rectopexy[62].

Madbouly *et al*[63] compared LRR with laparoscopic posterior rectopexy in 35 patients with rectal prolapse. The choice of operation depended on the symptoms: patients with constipation or normal bowel habits underwent LRR, patients with incontinence LPR. Constipation was improved in 90% of patients after LRR and incontinence was improved in 80% after LPR. This emphasizes the need to consider the underlying symptoms besides the morphologic alterations in the choice of procedure.

Raftopoulos *et al*[64] conducted a retrospective multicentre pooled data-analysis on 645 patients with rectal prolapse in order to determine the impact of the surgical approach and the method of rectopexy on recurrence rates (464 open, 179 laparoscopic operations). Used techniques were LPR, LRR, LSR or mobilisation only. They found recurrent rates from 20%-30% after a ten-year follow up irrespective of what operation method was used. A limitation of the study was the heterogeneity of the data with a variation of recurrence rates between the centres from 0% to 85%.

The limited data allows only modest conclusions: (1) rectopexy and resection rectopexy show equivalent functional outcome with a slight advantage of resection rectopexy in the improvement of constipation; (2) resection rectopexy leads to an increase of minor complications; (3) rectopexy should be performed in any case, as recurrence rates are higher if only rectal mobilisation is performed; and (4) recurrence rates do not differ between the procedures and reach 20% when a long term follow-up (about 10 years) is conducted.

LAPAROSCOPIC RECTOPEXY IN ELDERLY PATIENTS

It is thought that the group of elderly patients especially profits from laparoscopic surgery. A recent systematic review showed significant advantages in short term outcome in laparoscopic colorectal surgery for elderly people[65]. As the incidence of rectal prolapse and pelvic floor disorders increases with age it is important to know if laparoscopic procedures are safe for this group of patients and if they offer a good alternative to perineal procedures.

For ventral rectopexy a recent French study evaluated 4303 patients from a national database. Patients aged more than 70 years were compared to patients younger than 70 years. Elderly patients had more minor complications (urinary, wound complications) and a longer hospital stay, but major complication rate and mortality were not different[66]. Another study used a modified laparoscopic Orr-Loygue technique in 46 elderly patients (median age 83 years) with rectal prolapse. A significant cardiac morbidity was observed. Two patients died of cardiac arrest. Two patients were re-operated for recurrent prolapse after 2 mo. The reasons for the recurrences were mesh dislocations. Faecal incontinence improved significantly (Wexner-Score decreased from 19 to 5 points after one year). Constipation did not improve. Most patients were satisfied with the operation, but there was no association seen between satisfaction and functional result[67].

A German study from 2012 studied the outcome of LRR in elderly patients (> 75 years). The complication rate was slightly increased compared to the younger population. Incontinence and constipation improved in half of the patients irrespectively of age[68].

Dryberg used a laparoscopic dorsal mesh rectopexy in 81 older patients with FRP[69]. A remarkable major complication rate of 14.8% was reported. Port site hernias with consecutive ileus and postoperative haemorrhage each occurred in 5% of patients. Thirteen point five percent of recurrences were observed at a median follow-up of 2 years.

TYPICAL COMPLICATIONS AND THEIR MANAGEMENT

A study in a tertiary referral centre analysed the typical complications after mesh rectopexy: Mesh fistulation or erosion of the rectum, vagina or the bladder, recto-vaginal fistula, early symptomatic recurrence, rectal stricture and chronic pelvic pain were observed. In this study all complications could be managed laparoscopically[70].

The reasons for early recurrence were in all 27 cases an inadequate technique during the prior operation (only limited or no ventral dissection, no sutures in the recto-vaginal space, detachment or incorrect position of the staples, wrong placement of the mesh to the lateral instead the anterior rectal wall with development of an enterocele). These cases were treated by placement of a new mesh and fixation with staples and sutures. Recto-vaginal fistulas were treated with removal of the mesh and abdominal or transvaginal fistula repair. Rectal injuries and strictures were operated by anterior resection and a placement of a bio-mesh. In all patients with rectal strictures the mesh had been stapled to the mid-sacrum rather than to the promontory. Erosions of the vagina or the bladder were managed by mesh removal, defect repair and insertion of a bio-mesh. All women with this complication were postmenopausal and had previous hysterectomy. In patients that complained about chronic pain unresponsive to pain medication, the mesh showed an excessive inflammation. A replacement of the mesh by a teflon-coated mesh improved symptoms. After revisional surgery, quality of life and bowel function improved significantly.

Two case reports describe a mesh fistulation in the rectum[71,72]. Typical symptoms were recurrent fever, pelvic pain and rectal bleeding. Diagnosis was made

by flexible sigmoidoscopy. In one case therapy was anterior rectum resection, in the other case the mesh was extracted laparoscopically and a loop-ileostomy was performed.

Tranchart *et al*[73] observed 6 rectal mesh migrations after 312 laparoscopic ventral mesh rectopexies (1.9%). The median time interval between surgery and onset of symptoms was 53 mo (range 4 to 124 mo). The treatment was transanal partial mesh resection, in one case where a recto-cutaneous fistula was present, a deviating colostomy was added. A recurrent mesh migration was again treated with partial mesh resection. After a median follow-up of 40 mo all patients were free of complaints and showed no recurrent mesh, migration.

As a rare but serious complication lumbosacral discitis at the site of rectal fixation was observed after ventral rectopexy and resection rectopexy. Only four cases are reported in literature. Patients presented typically 1 to 3 mo after the initial operation with severe lower back pain, fever and malaise. An magnetic resonance imaging revealed the diagnosis. A contrast enema was helpful to rule out a rectal fistula. Broad spectrum iv-antibiotics covering colonic flora are the treatment of first choice. In some cases, antibiotic treatment was not sufficient, and removal of mesh or suture material was necessary, in one case with a deviating colostomy[31,74,75]. A gynaecological review found 26 cases of discitis after sacrocolpopexy or rectopexy in a 50-year period[76]. Although this complication is rare it should always be considered in patients complaining of persisting back pain after any type of rectopexy.

FINANCIAL CONSIDERATIONS

An Australian study from 2004 conducted a cost-effectiveness analysis for posterior mesh rectopexy in a randomised setting. When costs for theatre time, staff, laparoscopic equipment and hospital stay were included, the laparoscopic operation was less costly than the open operation. The shorter hospital stay in the laparoscopic group accounted for this saving[77].

ASSESSMENT OF DIFFERENT APPROACHES

The evaluation of the different operation techniques is difficult, as the quality of available studies is low and outcome parameters are not defined consistently.

Regarding complications and conversion rates all laparoscopic procedures provide similar good results with each having their typical complications (anastomotic leakage, mesh complications). Recurrence rates for all methods are below 10% within a follow-up of up to 5 years but studies that extended follow-up to 10 years found recurrence rates of up to 20%.

LRR and LVR improve both constipation and faecal incontinence in a similar degree, but randomised studies are missing. LSR and LPR have about the same effect on incontinence, but they tend to have a lesser effect on constipation, in some studies these operations even worsened constipation in a relevant number of patients.

As high quality evidence is missing, an individualized approach is recommend for every patient considering age, individual health status and the underlying morphological and functional disorders. Moreover, as most operations actually show acceptable results, the choice of procedure also depends on the experience and learning curve of the surgeon.

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P- Reviewer: Carter D, Song CJ
S- Editor: Ma YJ **L- Editor**: A **E- Editor**: Jiao XK

World Journal of Gastrointestinal Endoscopy

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Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
DOI: 10.4253/wjge.v7.i12.1055

World J Gastrointest Endosc 2015 September 10; 7(12): 1055-1061
ISSN 1948-5190 (online)

REVIEW

Coagulation syndrome: Delayed perforation after colorectal endoscopic treatments

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Author contributions: Hirasawa K designed and drafted of the article, and contributed to analysis and interpretation of data; Sato C, Makazu M, Kaneko H, Kobayashi R and Kokawa A contributed to acquisition of previous reports; Maeda S critically revised and finally approved of the article.

Conflict-of-interest statement: The authors declare no conflicts of interest regarding this manuscript.

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Received: April 28, 2015
Peer-review started: May 1, 2015
First decision: June 1, 2015
Revised: June 18, 2015
Accepted: August 30, 2015
Article in press: August 31, 2015
Published online: September 10, 2015

Abstract

Various procedure-related adverse events related to colonoscopic treatment have been reported. Previous studies on the complications of colonoscopic treatment have focused primarily on perforation or bleeding. Coagulation syndrome (CS), which is synonymous with transmural burn syndrome following endoscopic treatment, is another typical adverse event. CS is the result of electrocoagulation injury to the bowel wall that induces a transmural burn and localized peritonitis resulting in serosal inflammation. CS occurs after polypectomy, endoscopic mucosal resection (EMR), and even endoscopic submucosal dissection (ESD). The occurrence of CS after polypectomy or EMR varies according previous reports; most report an occurrence rate around 1%. However, artificial ulcers after ESD are largely theoretical, and CS following ESD was reported in about 9% of cases, which is higher than that for CS after polypectomy or EMR. Most cases of post-polypectomy syndrome (PPS) have an excellent prognosis, and they are managed conservatively with medical therapy. PPS rarely develops into delayed perforation. Delayed perforation is a severe adverse event that often requires emergency surgery. Since few studies have reported on CS and delayed perforation associated with CS, we focused on CS after colonoscopic treatments in this review. Clinicians should consider delayed perforation in CS patients.

Key words: Endoscopy; Syndrome; Colorectal; Dissection; Coagulation

Core tip: Few studies have reported on coagulation syndrome (CS) and delayed perforation associated with CS. Thus, in this review, we focused on CS after

colonoscopic treatments. CS is found in around 1% of cases after polypectomy and endoscopic mucosal resection and in 7%-8% of cases after endoscopic submucosal dissection. The prognosis for CS is excellent. However, clinicians should be mindful of delayed perforation in CS patients.

Hirasawa K, Sato C, Makazu M, Kaneko H, Kobayashi R, Kokawa A, Maeda S. Coagulation syndrome: Delayed perforation after colorectal endoscopic treatments. *World J Gastrointest Endosc* 2015; 7(12): 1055-1061 Available from: URL: http://www.wjgnet.com/1948-5190/full/v7/i12/1055.htm DOI: http://dx.doi.org/10.4253/wjge.v7.i12.1055

INTRODUCTION

Various endoscopic treatments such as polypectomy, endoscopic mucosal resection (EMR), and endoscopic submucosal dissection (ESD) have been used to treat colorectal neoplasms[1-14]. Colonoscopic polypectomy reduces the incidence of colorectal cancer by 70%-80%, and it has been used worldwide[1,2]. EMR is indicated for the treatment of colorectal adenomas, intramucosal, and submucosal superficial cancers (SM1; invasion of < 1000 μm from the muscularis mucosae) because of the negligible risk of lymph-node metastasis and excellent clinical outcomes; however, there is a limit to the size of *en bloc* resection[3-11].

Recently, ESD is another procedure used to remove large colorectal lesions according to the EMR curative criteria. This procedure is frequently used for removing large lesions by *en bloc* fashion, which includes lesions that would require piecemeal EMR for removal[11-14].

With respect to these aforementioned procedures, various procedure-related adverse events have been reported. Serious complications included delayed bleeding and perforation. Previous studies on the complications of colonoscopic polypectomy or EMR have primarily focused on perforation or bleeding[15-17]. Coagulation syndrome (CS) following endoscopic treatment, which was first reported as post-polypectomy syndrome (PPS)[18], is another typical complication. This has syndrome has a variety of names, including post-polypectomy CS, post-polypectomy electrocoagulation syndrome, and transmural burn syndrome[17-33]. Recognizing CS is important to avoid unnecessary exploratory laparotomy, because the syndrome can resolve with conservative treatment in most patients[19,21,23,26,30,31]. However, little is known about the clinical characteristics, clinical outcomes, and risk factors associated with CS, and the frequency of CS varies in previous studies[17-33]. Additionally, CS occurs after polypectomy, EMR, and even ESD[26,34]. With the evolution of treatment, the occurrence of this syndrome is thought to increase. Furthermore, there is a possibility that CS causes delayed perforation, which is a very severe complication[25,26,33,35-42]. In this review, we clarify the present status of CS following endoscopic treatment for colorectal neoplasms.

Most previous studies have investigated CS after polypectomy and EMR. Thus, in this review, we defined PPS as CS associated with only polypectomy and EMR, while CS included ESD.

DEFINITION OF CS

CS is the result of an electrocoagulation injury to the bowel wall that induces a transmural burn and localized peritonitis resulting in serosal inflammation[17-33]. Patients with CS are diagnosed when they present with abdominal pain (sometimes tenderness with rebound); fever; leukocytosis; an elevated C-reactive protein level; or peritoneal irritation symptoms and signs that occur after colonoscopic treatment (polypectomy, EMR, and ESD) with electrocoagulation, in the absence of visualized perforation by abdominal radiography and/or computed tomography (CT)[26,34]. It is important to recognize that CS can be misleading, as it can resemble a true rupture of the colon and present with pain, a low fever, and mild leukocytosis. Typically, patients with CS present within a few hours to 7 d after colonoscopic treatment with fever, localized abdominal pain, and localized peritoneal signs[19,20,26,30]. It is important to recognize this condition, because it does not require surgical treatment in most cases[19,21,23,26,30,31]. There is a range in severity of PPS between admission to the intensive care unit and post-discharge, as it can lead to shock, additional surgery, or death from possible follow-up on an outpatient basis.

CLINICAL CHARACTERISTICS

The rate of occurrence

The occurrence rate of PPS varies widely from 0%-7.6% in previous reports; however, most studies report a rate around 1%. It is considered some reports had high percentages of occurrence due to small patient populations[18-21,23-26,28-33].

Risk factors

Some previous reports have investigated the risk factors of PPS Nivatvongs[18] showed that 83% of PPS patients had polyps in the right side of the colon, and all were sessile polyps. Choo *et al*[24] also showed that right-colon polypectomies had a statistically significantly higher tendency for developing PPS. Lee *et al*[20] reported that a polyp size > 2 cm (OR = 1.08) and hypertension (OR = 14.40) were associated with a significantly increased risk of PPS. The most recent report showed that hypertension, a large lesion size, and non-polypoid configuration of the lesion were independently associated with PPS according to multivariate analysis[19].

PPS develops when the electrical current applied during colonoscopic polypectomy extends past the mucosa into the muscularis propria and serosa, resulting in a transmural burn without perforation[17-33]. Therefore, larger lesions and non-polypoid configuration are logical

risk factors, as they usually require a large amount of thermal energy for a longer duration. However, the mechanism of hypertension to promote PPS is unclear. Patients with hypertension are more likely to have endothelial dysfunction[43] and atherosclerosis[44,45], which may be contributing factors.

However, with thinness of the wall, there is also concern regarding the frequency of PPS. The right colon wall is thin, and a large study that addressed major post-polypectomy complications reported barotraumatic perforations, and all of them were caused by cecal blow-out[34,46-48]. Regarding colonic perforation, it has been suggested that air insufflation during colonoscopy generates a higher pressure in the cecum than in the rest of the colon, increasing vulnerability to injury. In addition, Rutter *et al*[49] hypothesized that a more perpendicular approach to polypectomy in the cecum may increase the risk of complications. However, scientific evidence in support of these theories is lacking.

Loffeld *et al*[47] also reported that barotrauma caused by insufflated air occurs more often than therapeutic perforation due to polypectomy or coagulation.

Prevention of PPS

Theoretically, submucosal saline injections of large, non-polypoid lesions prior to EMR may reduce the risk of PPS. The rationale for this is that a submucosal saline injection may increase the thickness of the submucosal layer and consequently reduce the risk of PPS[32]. However, no studies have supported this assumption. Sethi *et al*[17] hypothesized that submucosal injection itself leads to serosal irritation and localized peritonitis, and then patients present with PPS symptoms. Therefore, the protective role of the saline "cushion" for PPS should be considered in future studies.

The improvement of devices would likely reduce PPS. Galloro *et al*[50] reported that steel snares induced significantly deeper tissue injury than tungsten snares in the pure cut mode; therefore, tungsten snares may reduce the risk of PPS[32]. Another way to reduce the risk of PPS is dependent on skill. Using lower risk procedures when clinically appropriate or referring patients to high-volume endoscopists can reduce the complication rates[51].

PPS is considered different from infection from a local mucosal defect. Min *et al*[52] reported that blood cultures at baseline and 5 min after the procedure were all negative, and a blood culture at 30 min after the procedure showed a positive result in only 1 of 40 patients (2.5%). However, this one positive sample was considered contamination. None of the 40 patients showed any signs or symptoms associated with infection. Therefore, the prior administration of antibiotics is considered controversial for preventing PPS.

Treatment and prognosis

Most cases of PPS have an excellent prognosis, and they are managed conservatively with medical therapy. In some reports, all patients were admitted to the hospital, while in other reports, some cases underwent outpatient observation[19,21,23,26,30,31]. Treatment of PPS requires bowel rest and the administration of intravenous fluids and broad-spectrum parenteral antibiotics to cover the colonic bacterial flora. Nothing is taken by mouth until the symptoms subside. Patients with mild symptoms and adequate outpatient follow-up can be managed with oral antibiotics and a clear liquid diet for 1-2 d.

In contrast, to diffuse peritoneal signs, there is an indication for immediate surgical intervention. Within the spectrum of post-polypectomy cautery injury, "mini-perforation" falls between a "serosal burn" and frank perforation (with diffuse peritonitis). It is a minimal defect that can be quickly covered by peri-intestinal fat and omentum[16]. Its clinical features include pneumoperitoneum without signs and symptoms of diffuse or spreading peritonitis, and with local tenderness that is characteristic of a full-thickness burn. The patient usually improves within 24 h, and the symptoms should resolve within 96 h with conservative treatment. The dilemma as to whether the conservative or surgical approach is more appropriate for managing this kind of perforation still exists[19-22,26,30,31].

Although conservative treatment can generally be performed in most patients, it is important to adopt careful measures such as prolonging the fasting period and considering the possibility of delayed perforation[26,35-39].

DELAYED PERFORATION

Immediate perforation is diagnosed by endoscopy during resection and by the presence of free air on plain abdominal film or abdominal CT scan[15-17,35,51,53]. This is very rare; however, delayed perforation, which is considered to be caused by an electrical or thermal injury after electrocoagulation, was reported in these cases. Delayed perforation after colonoscopic resection can begin as PPS, which can evolve into a perforation or as a free perforation with air and fluid leakage, resulting in pneumoperitoneum and peritonitis[35-39].

Japan Gastroenterological Endoscopy Society guidelines for colorectal ESD/EMR defined delayed perforation as an intestinal perforation that develops over a certain period postoperatively (*i.e.*, intestinal perforation that is detected after the scope has been withdrawn following completion of ESD/EMR during which perforation did not occur). This is diagnosed based on abdominal pain, abdominal findings, the presence of a fever, and an inflammatory response that is consistent with PPS. Most cases of delayed perforation occur within 14 h after endoscopic resection. However, approximately one-third of delayed perforation cases are confirmed within 24 h after treatment. Free air, which cannot be detected by simple radiographic imaging, is sometimes found on abdominal CT. Therefore, in cases where delayed perforation is suspected, abdominal CT should be performed. Surgeons must be called for emergency surgery, because it is essential in cases of delayed perforation[26].

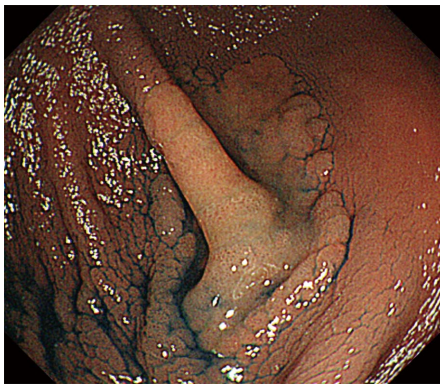

Figure 1 Chromoendoscopy showing a 30 mm laterally spreading tumor (non-granular type) located at the bottom of the cecum bottom.

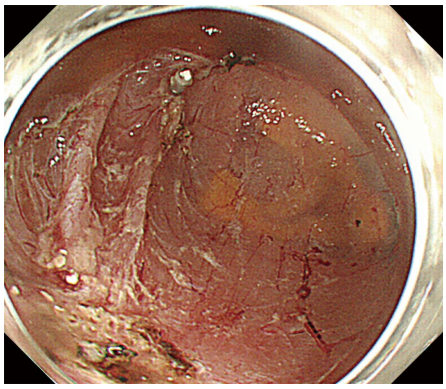

Figure 2 Endoscopic submucosal dissection is performed safely without intraoperative perforation. The procedure time is 47 min.

In 1994, Lo *et al*[54] reported that 43.8% of therapeutic perforations were managed conservatively with a mortality rate of 4.1%. This means that perforation is still a severe condition that reduces patients' quality of life[25,35-39]. Thus, prevention of PPS and its potential sequelae are most important, and clinicians must always consider the potential for delayed perforation due to PPS.

Only two studies have reported on the incidence of delayed perforation. Taku *et al*[39] reported delayed perforation in 7 of 15070 cases, while Waye *et al*[25] reported it in 1 of 777 cases. This is still not sufficient evidence. For ESD, the incidence of delayed perforation ranges from 0.1% to 0.4%[26,40-42].

THE RELATIONSHIP WITH ESD

CS after ESD

ESD has been a reliable method for en bloc resection of colorectal tumors regardless of the lesion size for years. Although colorectal ESD has been established as a procedure with reproducible safety and efficacy, complications such as intestinal perforation and delayed bleeding remain to be problematic. Similarly, few studies have reported CS after ESD[11-14,26].

Hong *et al*[48] reported that 8.6% showed CS after colorectal ESD. There were no differences in the demographic and endoscopic characteristics (age, sex, underlying disease, procedure time, tumor size, macroscopic type, location, and pathologic findings) between patients with CS and those without CS. The mean hospitalization stay was statically significantly longer in the CS group than that in the non-CS group. All patients with CS were treated with conservative (non-surgical) management (*e.g.*, fasting and intravenous antibiotics). CS showed a favorable progression even after ESD, and delayed perforation was not reported. See comment in pubmed commons below.

Delayed perforation after ESD

CS is reported even after ESD, and its frequency is clearly higher than polypectomy or EMR[26,34,48]. The procedure time and ulcer bed to energization that largely affects the characteristics of ESD procedures is evident theoretically. Delayed perforation in ESD is also a great concern. The indications for ESD are markedly different from those for conventional EMR, and the overall perforation rate is higher compared to conventional EMR[55]. Delayed perforation after ESD reportedly ranges from about 0.1%-0.4%; however, this may be because of the small number of reports[26,40-42,55].

Saito *et al*[41] reported that delayed perforations occurred in another 4 patients (0.4%) after ESD. Two of the 4 patients with delayed perforations were successfully treated conservatively, because the abdominal findings and inflammatory changes based on laboratory data were slight. However, other patients with delayed perforation required emergency surgery because of the risk of peritonitis. Saito *et al*[41] also reported that 0.11% (1/900) showed delayed perforation that required emergency surgery. Previous studies have cautioned that clinicians must carefully follow patients with delayed perforation, and continually close communication with consulting surgeons is essential since the number of such cases has been quite limited to date.

Few studies have reported on delayed perforation after ESD. While previous reports have shown the success of endoscopic clip closure with over-tube[42], the treatment and prognosis often require emergent surgery.

Case presentation

A 44-year-old woman underwent colonoscopy for surveillance of ulcerative colitis, and a 30 mm cecal sessile polyp was revealed (Figure 1). We diagnosed this tumor as a sessile serrated adenoma/polyp using the pit and narrow-band imaging patterns. Because of the size of the tumor and the tumor morphology, we chose ESD in order to perform en-bloc resection. ESD was performed safely without any perioperative complications (Figures 2 and 3), and she reported no symptoms. However, 24 h after ESD, she had a high fever (38.6 ℃) with slight abdominal pain and leukocytosis. Subsequently, she was diagnosed with CS after ESD. She fasted and received

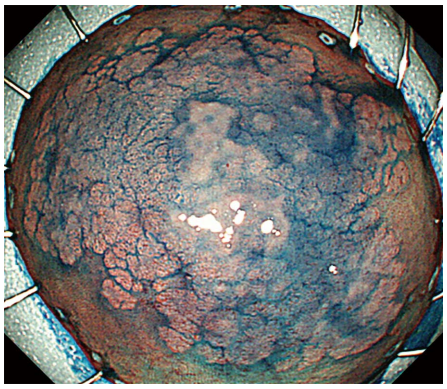

Figure 3 The tumor is resected in an *en bloc* fashion, and the specimen measures 51 mm × 40 mm.

Figure 4 Abdominal contrast enhanced computed tomography 24 h after endoscopic submucosal dissection. Free air is not recognized.

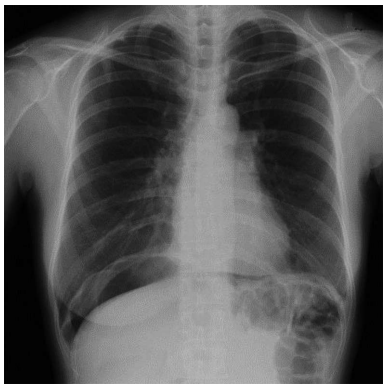

Figure 5 Abdominal radiography 36 h after endoscopic submucosal dissection because of a complaint of severe abdominal pain. A large amount of free air is observed under the diaphragm.

antibiotics (cefmetazole). CT was obtained immediately, but no findings were suggestive of perforation (*i.e.*, free air and ascites were not present) (Figure 4). Thirty hours after ESD, severe abdominal pain developed, and 36 h after ESD, free air appeared on radiography and CT (Figures 5 and 6). At this point, we diagnosed the patient with delayed perforation that developed after CS. Emergent laparoscopic surgery was performed, and a perforation site was found in the ESD ulcer at the bottom

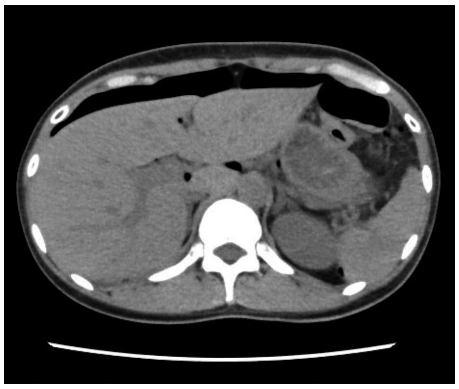

Figure 6 Abdominal computed tomography 36 h after endoscopic submucosal dissection. A large amount of free air is observed on the surface of the liver and the intraperitoneal cavity.

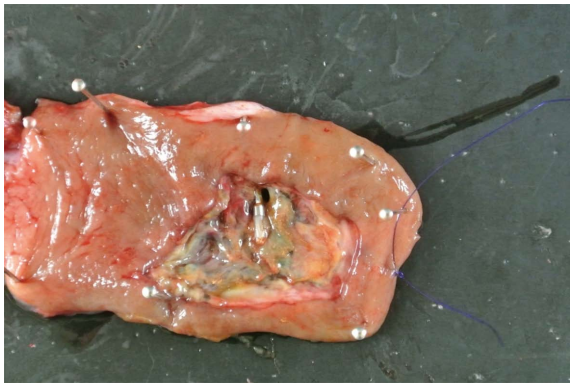

Figure 7 A small perforation site is present in the surgical specimen.

of the cecum (Figure 7). Partial cecum resection was performed, and the patient's condition improved rapidly.

CONCLUSION

CS is found in around 1% of cases after polypectomy and EMR and in 7%-8% of cases after ESD. Although the prognosis is excellent, clinicians should consider delayed perforation in CS patients.

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P- Reviewer: Kozarek R
S- Editor: Qiu S **L- Editor**: A **E- Editor**: Jiao XK

World Journal of Gastrointestinal Endoscopy

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DOI: 10.4253/wjge.v7.i12.1062

World J Gastrointest Endosc 2015 September 10; 7(12): 1062-1069
ISSN 1948-5190 (online)

Treatment modalities for early gastric cancer

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Author contributions: All authors contributed equally to the paper.

Conflict-of-interest statement: The authors declare that they have no competing interests.

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Received: April 25, 2015
Peer-review started: April 26, 2015
First decision: June 2, 2015
Revised: June 17, 2015
Accepted: August 25, 2015
Article in press: August 28, 2015
Published online: September 10, 2015

Abstract

Different treatment modalities have been proposed in the treatment of early gastric cancer (EGC). Endoscopic resection (ER) is an established treatment that allows curative treatment, in selected cases. In addition, ER allows for an accurate histological staging, which is crucial when deciding on the best treatment option for EGC. Recently, endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) have become alternatives to surgery in early gastric cancer, mainly in Asian countries. Patients with "standard" criteria can be successfully treated by EMR techniques. Those who meet "expanded" criteria may benefit from treatment by ESD, reducing the need for surgery. Standardized ESD training system is imperative to promulgate effective and safe ESD technique to practices with limited expertise. Although endoscopic resection is an option in patients with EGC, surgical treatment continues to be a widespread therapeutic option worldwide. In this review we tried to point out the treatment modalities for early gastric cancer.

Key words: Early gastric cancer; Endoscopic submucosal dissection; Endoscopic mucosal resection; Pathological staging; Gastrectomy

Core tip: Gastric cancer is one of the main causes of cancer death. For early gastric cancer (EGC) endoscopic resection is an effective treatment modality for selected cases of EGC. Endoscopic submucosal dissection is designed to provide *en bloc* R0 resection regardless of size. Gastrectomy is the standard treatment for EGC with suspected lymph node metastases. This review describes the current different treatment modalities for early gastric cancer.

Espinel J, Pinedo E, Ojeda V, Guerra del Rio M. Treatment modalities for early gastric cancer. *World J Gastrointest Endosc* 2015; 7(12): 1062-1069 Available from: URL: http://www.wjgnet.com/1948-5190/full/v7/i12/1062.htm DOI: http://dx.doi.org/10.4253/wjge.v7.i12.1062

INTRODUCTION

Gastric cancer is one of the leading causes of cancer worldwide, causing high mortality. In Asian countries, the frequency of early gastric cancer (EGC) is far superior to that of Western countries. Currently early gastric cancer (EGC) is defined as one that is limited to the mucosa or submucosa, regardless of the existence of nodal metastases[1]. The incidence of lymph node metastasis in EGC is very low. If the EGC is confined to the mucosa, the incidence is estimated at around 3%. When the EGC reaches the submucosa, rises to nearly 20%[2]. The existence of nodal metastases influence the type of treatment to be used. In these cases, surgical treatment is recommended along with adjuvant therapy. Overall the EGC has a good prognosis, with a 5-year survival rate of over 90%[3]. There are different therapeutic options for the treatment of early gastric cancer. At present, endoscopic resection provides a minimally invasive treatment with a similar efficacy to surgery.

TREATMENT MODALITIES

Therapeutic modalities for EGC range from endoscopic resection to gastrectomy and adjuvant treatments. Therefore, it is essential to perform an adequate staging of cancer as to determine which patients are candidates for either therapy.

ENDOSCOPIC TREATMENT

Endoscopic therapy is a minimally invasive treatment that allows the patient to preserve the entire stomach and maintain a good quality of life. Moreover, the cost is usually less and efficacy comparable to surgery. The degree of difficulty in performing endoscopic resection depends on the location of the lesion in the stomach, being the difficulty higher for resection of lesions localized on the posterior wall and lesser curvature. Depressed type of EGC is the most common. To facilitate the visualization of the lesion mucolytic and defoaming agents are used (*e.g.,* Acetylcysteine and Dimethicone, respectively). Endoscopic therapy is directed to selected patients in whom there is no evidence or risk of lymph node involvement. Endoscopic resection *vs* ablative technique allows assessing the specimen thus becoming the optimal method of staging for early gastric cancer[4]. Also, endoscopic therapy does not prevent a subsequent surgical therapy if needed. EUS has limited staging accuracy (80%-90%) and therefore would result in unnecessary surgery in up to 10%-20% of patients[5,6]. Endoscopic resection allows the pathologist to assess the depth of invasion, degree of differentiation and lymphatic and vascular involvement, thus allowing for a prediction of the risk of metastases in the lymph nodes. This is crucial for a correct diagnosis and risk stratification of metastasis. The main endoscopic techniques used are endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD). According to the histological and morphological findings gastric carcinoma can be divided into differentiated (intestinal) and undifferentiated (diffuse)[7]. The risk for nodal metastasis for differentiated and undifferentiated EGC is around 0.4% and 4%, respectively. Endoscopic resection techniques can be applied, according to "standard" criteria, in patients with lesions resectable *en bloc* which meet histological criteria (intestinal type adenocarcinoma limited to the mucosa without venous or lymphatic invasion) and morphological criteria (< 20 mm without ulceration; < 10 mm for flat and depressed lesions)[8,9]. When these criteria are met, the risk of lymph node involvement is not more than 1.7%. In addition, "expanded" criteria for endoscopic resection have been defined which include: (1) EGC intestinal type mucosa confined to any size without ulceration; (2) EGC intestinal type confined to the mucosa < 3 cm with ulceration; and (3) EGC intestinal type < 3 cm confined to the upper 0.5 mm from the submucosa (sm1 < 500 μm) without lymphovascular involvement and 4. ECG poorly differentiated, < 2 cm, not ulcerated[10,11]. Expanded criteria for ER reduces the need for gastrectomy in EGC (Table 1). When ER has been performed for poorly differentiated type of EGC results for patients who declined surgical treatment showed: *en bloc* resection rate 83%, complete resection rate 81%, clinical remission 93%, and recurrence in only 7%[12].

Endoscopic mucosal resection

Currently endoscopic mucosal resection (EMR) is considered as an effective and safe treatment for superficial lesions. Requires specific endoscopic experience and the endoscopist needs to be prepared to try to resolve the possible complications that may arise during the implementation of the technique. Over the last years different EMR techniques have been described[13]: (1) Strip biopsy[14]. This resection technique designed to remove small lesions requires the use of a dual channel endoscope. It simultaneously uses a polypectomy snare and a biopsy forceps to achieve the resection; (2) Endoscopic double snare polypectomy; (3) EMR using a transparent plastic cap, initially developed in 1992 for resection of early oesophageal cancer and later for resection of early gastric cancer[15]; and (4) EMR using a ligation device (Multiband mucosectomy)[16,17] (Figure 1). These last two are the techniques for endoscopic mucosal resection most widely used in the treatment of EGC. However, in lesions greater than 20 mm, recurrence rate may be increased as they might require a piecemeal resection[18]. Therefore, EMR is the procedure of choice in patients with EGC who meet the standard criteria for endoscopic resection. Different studies have shown excellent results using EMR with figures for complete resection and survival at 5 years greater than 85%-90%[19,20]. The risk of local recurrence associated with EMR is variable. If the resection is piecemeal the risk of recurrence rate is set below 35%,

Table 1 Treatments options in a patient with early gastric cancer

Histology	Mucosal cancer					Submucosal cancer	
	⩽ 10 mm (flat/depressed)	⩽ 20 mm > 20 mm (No ulceration)		⩽ 30 mm > 30 mm (Ulceration)		Into the upper third (⩽ 30 mm)	Into the middle third (any size)
Intestinal type	EMR	EMR	ESD	ESD	Surgery	ESD	Surgery
Diffuse type	Surgery ESD[1]		Surgery	Surgery	Surgery	Surgery	Surgery

[1]Treatment option if the patient decline surgery. EGC: Early gastric cancer; EMR: Endoscopic mucosal resection; ESD: Endoscopic submucosal dissection.

Table 2 Process steps in endoscopic submucosal dissection treatment of the early gastric cancer

Process steps	Technique/devices
Estimation of lateral extension	Chomoendoscopy (indigo carmine) ± NBI
Marking	Mucosal markings are placed 5 mm lateral to the lesion margin
Submucosal injection	Injection of saline mixed with diluted epinephrine (1:100000) and indigo carmine into the submucosal layer
Mucosal incision (precutting)	A small initial mucosal incision is made to gain access to the submucosal space without to injure the muscularis propria (*e.g.*, by Dual knife)
Circumferential incisión	Carried out 5 mm lateral to the mucosal markings (*e.g.*, IT knife)
Submucosal dissection	The technique varies among endoscopist Adequate reinjection of fluid into the submucosa The parallel movement for muscle layer with the IT2 is typically lateral With the Dual knife forward

NBI: Narrow band imaging.

being practically nonexistent if *en bloc* resection was possible[21,22]. In cases of incomplete resection with EMR, gastrectomy might be indicated if the tumor has submucosal or lymphovascular involvement or positive resection margins. However, in cases where the patient is a poor surgical candidate further endoscopic resection could be considered with good results, especially if incomplete resection is due to the presence of positive lateral margins of resection[23,24]. In treatment with EMR a suitable distance of at least 2 mm between the EGC and the edge of the specimen is required to achieve complete resection. Indigo carmine chromoendoscopy is the most useful method to determine the lateral margin of EGC.

Endoscopic submucosal resection

Endoscopic submucosal resection (ESD) is a complex and demanding technique that allows *en bloc* resection of larger EGC, avoiding piecemeal resection of the EMR and therefore the risk of recurrence[25-27]. Similar to the EMR, its main indication is resection of superficial tumors with no risk of lymph node metastasis. Expanded criteria have been proposed for endoscopic resection with ESD, as with this technique large *en bloc* resections are possible. ESD for EGC with expanded criteria have long-term survival and outcomes similar to those of patients treated according to the traditional criteria (5-year survival rate 93% and 92%, respectively)[28]. In ESD, the lesion is marked circumferentially, usually by applying soft coagulation current. Then, a solution with saline (0.9% NS), adrenaline and dyes (indigo carmine, methylene blue) is injected into the submucosa allowing distinction between the submucosal and muscular layer. Some authors do not recommend the use of Methylene blue because it is absorbed into the cell nucleus, which results in intense staining that hampers visualization[29]. To avoid the short duration of the lifting effect of submucosal injection, others have suggested the use of substances with a viscosity grade higher than saline (0.9% NS). The use of hyaluronic acid has been proposed but its high price, has conditioned its use[30,31]. Glycerol 10% could be a good and cheap alternative[32]. Finally, the lesion is dissected and removed *en bloc* using different types of needles, specific for each step of the procedure (Needle Knife, IT Knife, Flex knife, Hook knife, Triangle-tip knife, Dual Knife, Hybrid Knife, Flush knife and others) typically done with coagulating current. Some needles have at the tip an insulating material with a protective function that allows for a safer dissection[33-35] (Figure 2). The main functions that must meet the ESD devices are: marking, injection, precutting, circumferential incision, submucosal disection and hemostasis (Table 2). However the choice of needle depends on the availability, familiarity and personal preference of the endoscopist as there are no studies that demonstrate the superiority of one over the other. Sometimes it can be useful to use a transparent plastic cap on the endoscope tip that allows more control during dissection. Moreover, these devices use cutting currents, coagulation or a mixture of both through electrosurgical generators. CO_2 insufflation is recommended because it causes less luminal distension. Furthermore, if there is a perforation the leaking CO_2 will rapidly be reabsorbed decreasing the intraperitoneal pressure and then the respiratory compromise[36]. From a technical point of view, ESD is more challenging than EMR and requires

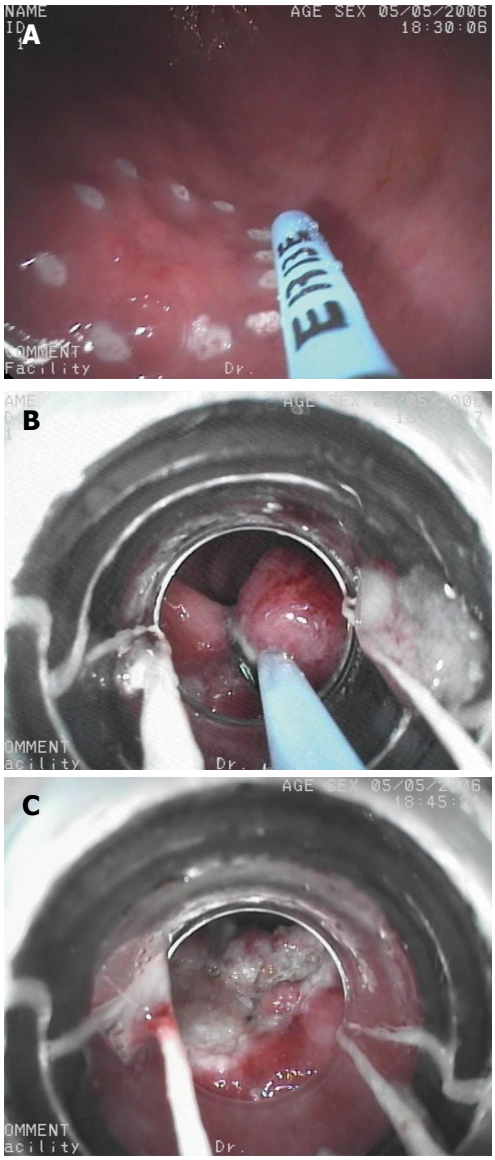

Figure 1 Endoscopic mucosal resection with Multiband Ligator for early gastric cancer. A: Argon plasma coagulation is used for marking early gastric cancer; B: A multiband ligator was used to create a pseudopolyp and it is removed by a minipolypectomy snare using pure coagulating current; C: Residual scar after Multiband Mucosectomy.

more "preparation". However, the main advantage of the ESD over other techniques is that it allows *en bloc* resection of larger lesions reducing the rate of local recurrence. As demonstrated in comparative studies between EMR and ESD, with ESD success rates between 95%-98% for in-bloc resection and survival at 5 years of 83%-97%[37,38]. The ESD requires skill and a long learning curve[39-42]. In cases when resection with ESD is incomplete (positive resection margins, invasion of the submucosa or muscularis, lymphovascular invasion or undifferentiated cancer), surgery should be considered (gastrectomy with perigastric nodal resection)[43]. The role of laparoscopic perigastric nodal resection is not clearly established but may be considered as an alternative[44]. ESD can be use in elderly patients as well as in those who require antiplatelet therapy for high risk of thrombosis[2]. Proposed strategy for endoscopic treatment by ESD set 4 levels: capability for EGC detection and knowledge of the indications of ESD, observation of several ESD procedures performed by expert endoscopists, perform dissections in *ex-vivo* animal models followed by procedures in animal models *in vivo* and finally performing selected (simple) ESD in humans under expert supervision. Then, continue with training in animal models to acquire more skill. About 20 annual cases of ESD are considered necessary to acquire competence in ESD[2]. In Japan and Korea the incidence of early gastric cancer is significantly higher compared to the West. Therefore in the West, the opportunities to conduct training in gastric EDS are scarce.

ENDOSCOPIC COMPLICATIONS

Various complications after endoscopic treatment for EGC have been described: bleeding, perforation, stenosis, aspiration pneumonia, phlegmonous gastritis, mediastinal emphysema. Of these, the most common is bleeding, the average incidence is set at 9% and usually occur during the process or within 24 h[45]. Depending on the time of onset, bleeding can be classified as: (1) immediate; (2) early (within the procedure); or (3) late (post-procedure). The immediate bleeding is less common in the distal portion of the stomach as the submucosal arteries are of lower caliber[46]. Acute bleeding may obscure the visual field, leading to a higher risk of complications. Therefore, endoscopic hemostasis should be immediately performed. The incidence of delayed bleeding after ESD is below 15%[37] and different factors have been related to its appearance: macroscopic appearance (large size > 40 mm, depressed or flat lesion), location in the middle or upper third, advanced age (> 80 years), limited endoscopic experience, timely procedure or treatment of recurrent lesions[47,48]. Late risk of bleeding after ESD may decrease significantly by prophylactic electrocoagulation of large visible submucosal vessels. This technique is preferable to other types of hemostasis such as clips that can hinder the completion of the procedure[49]. Currently, there is no evidence that the realization of a second-look contributes significantly to reduce the risk of late bleeding following ESD. While it is habitual to advice antisecretory therapy over the following weeks, this practice has not demonstrated benefit in lowering the rate of delayed bleeding[50]. The incidence of perforation ranges from 1%-20% depending on experience[51-53]. The use of dye injection (*e.g.,* Indigo carmine) allows to better identify the muscle layer making ESD a safer technique. Perforation can be diagnosed during or after the procedure (frank perforation or micro-perforation, respectively). However, no evidence of lymph node metastasis and/or peritoneal dissemination caused by gastric perforation has been reported[54]. If a perforation is immediately noticed during the procedure and its size is small, it can be treated endoscopically with clips

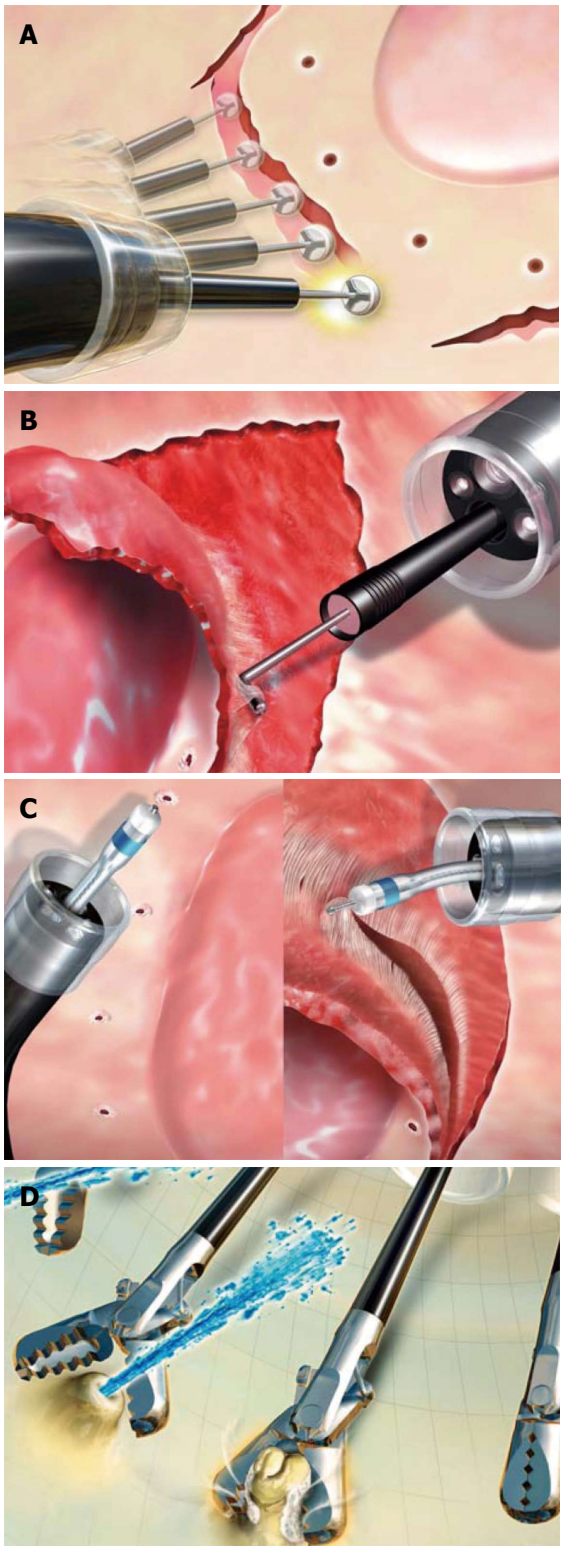

Figure 2 Different types of devices, specific for each step of the Endoscopic submucosal dissection procedure. A: ITknife-2; B: Hook knife; C: Dual knife; D: Grasper for haemostasis. (Courtesy of Olympus Medical Systems,Tokyo, Japan).

and broad spectrum antibiotics. In these cases absolute diet is recommended for at least 2 d[55]. Conversely, if the perforation is large, urgent surgery is required. It is possible that CO_2 insufflation may reduce the risk of perforation[56]. If free air is found on a plain chest X-ray after the ER (micro-perforation), the management (conservative or surgical) is not conclusively established. The appearance of scar stenosis is uncommon (0.6%-2%) and is associated with extensive resections in the gastric antrum[51]. Local administration triamcinolone can be used as an attempt to prevent this complication[57]. Balloon dilation is the endoscopic treatment most frequently used for this complication, but involves some risk of perforation[58]. Aspiration pneumonia is rare (0.7%-1.5%) and is associated with prolonged procedures.

FOLLOW-UP AFTER ENDOSCOPIC RESECTION

EGC patients treated by endoscopic resection with curative intent, require monitoring to detect local recurrence and metachronous gastric cancer. In patients with EGC who meet "standard" criteria for endoscopic resection, it is advisable to perform an upper gastrointestinal endoscopy yearly. Patients who meet "expanded" criteria, in addition to the annual endoscopy, monitoring can be performed alternating abdominal computed tomography and endoscopic ultrasound every 6 mo for 3 years. The objective of this additional monitoring is to detect lymph node and distant metastases[59].

SURGICAL TREATMENT

Although endoscopic resection is an option in patients with EGC who meet the above criteria, surgical treatment continues to be a widespread therapeutic option worldwide with survival rates at 5 years of 97%[60]. Currently, there are no comparative studies between gastrectomy and endoscopic treatment. However, several results show clinical prognosis to be similar although patients with endoscopic treatment benefit from a shorter hospital stay and lower costs[61,62]. Patients who do not meet the criteria for endoscopic resection have a higher risk of lymph node metastases which forces a gastrectomy with perigastric lymph node excision. Another indication for gastrectomy is the detection during staging of lymph nodes or a high suspicion of their existence. The type of gastrectomy (subtotal gastrectomy or total) is determined by the location of the lesion, reserving the subtotal gastrectomy for EGC located in the lower two thirds of the stomach. Another option is laparoscopic gastrectomy. Laparoscopic gastrectomy was initially reported in Japan in 1994[63]. Open gastrectomy is still performed more frequently in the Western countries than laparoscopic resection even for patients with early stage disease[64]. In Japan, EGC (T1N0 or T2N0) is considered as the only indication for laparoscopic gastrectomy. A recent review that included 22 studies show that laparoscopic gastrectomy *vs* open gastrectomy offers a similar prognosis with significantly lower postoperative morbidity, lower intraoperative

blood use, shorter hospital stay and no increased rates of recurrence. Furthermore conversion rates to open laparoscopic surgery were less than 3%[65].

The surgical outcome of gastric cancer in obese patients is controversial. The number of lymph nodes retrieved is, in these patients, higher[66]. Moreover, obesity is an independent risk factor for developing 30-d postdischarge complications[67].

ADJUVANT THERAPIES

It is known that chronic infection with *Helicobacter pylori* is a risk factor of developing gastric cancer. Currently, treatment of *Helicobacter pylori* infection in all patients with EGC is recommended, regardless of the chosen treatment option to reduce the risk of metachronous gastric cancer[68,69]. The need for adjuvant therapy (chemotherapy, radiotherapy) in patients with EGC treated with complete endoscopic resection is debated. Recent guidelines recommend observation, avoiding adjuvant therapy in patients with T1N0 disease without involvement of the resection margins. However, adjuvant treatment is clearly indicated in patients with positive lymph node involvement.

CONCLUSION

Endoscopic resection (EMR/ESD) is a safe and effective staging and therapeutic modality for selected patients with early gastric cancer. Patients with "standard" and "expanded" criteria can be successfully treated by EMR and ESD techniques, respectively. Surgical treatment continues to be a widespread therapeutic option in patients with incomplete endoscopic resection or advanced gastric cancer.

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P- Reviewer: Murata A, Tarantino G
S- Editor: Ma YJ **L- Editor**: A **E- Editor**: Jiao XK

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DOI: 10.4253/wjge.v7.i12.1070

World J Gastrointest Endosc 2015 September 10; 7(12): 1070-1077
ISSN 1948-5190 (online)

ORIGINAL ARTICLE

Retrospective Study

Diagnosis of small intramucosal signet ring cell carcinoma of the stomach by non-magnifying narrow-band imaging: A pilot study

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Jiro Watari, Toshihiko Tomita, Hisatomo Ikehara, Masato Taki, Tomohiro Ogawa, Takahisa Yamasaki, Takashi Kondo, Fumihiko Toyoshima, Jun Sakurai, Tomoaki Kono, Katsuyuki Tozawa, Yoshio Ohda, Tadayuki Oshima, Hirokazu Fukui, Hiroto Miwa, Division of Gastroenterology, Department of Internal Medicine, Hyogo College of Medicine, Nishinomiya, Hyogo 663-8501, Japan

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Institutional review board statement: This study was approved by Institutional Review Board at Hyogo College of Medicine, Nishinomiya, Japan.

Informed consent statement: All patients in the study gave informed consent prior to endoscopy.

Conflict-of-interest statement: None.

Data sharing statement: Technical appendix, statistical code, and dataset available from the corresponding author at (watarij@hyo-med.ac.jp). Consent for data sharing was not obtained from the participants but the presented data are anonymized and risk of identification is low.

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Received: April 10, 2015
Peer-review started: April 12, 2015
First decision: June 4, 2015
Revised: July 22, 2015
Accepted: August 13, 2015
Article in press: August 26, 2015
Published online: September 10, 2015

Abstract

AIM: To examine the efficacy of non-magnifying narrow-band imaging (NM-NBI) imaging for small signet ring cell carcinoma (SRC).

METHODS: We retrospectively analyzed 14 consecutive small intramucosal SRCs that had been treated with endoscopic submucosal dissection (ESD) and 14 randomly selected whitish gastric ulcer scars (control). The strength and shape of the SRCs and whitish scars by NM-NBI and white-light imaging (WLI) were assessed with Image J (NIH, Bethesda).

RESULTS: NM-NBI findings of SRC showed a clearly isolated whitish area amid the brown color of the

surrounding normal mucosa. The NBI index, which indicates the potency of NBI for visualizing SRC, was significantly higher than the WLI index (P = 0.001), indicating SRC was more clearly identified by NM-NBI. Although the NBI index was not significantly different between SRCs and controls, the circle (C)-index, as an index of circularity of tumor shape, was significantly higher in SRCs (P = 0.001). According to the receiver-operating characteristic analysis, the resulting cut-off value of the circularity index (C-index) for SRC was 0.60 (85.7% sensitivity, 85.7% specificity). Thus a lesion with a C-index $\geqslant$ 0.6 was significantly more likely to be an SRC than a gastric ulcer scar (OR = 36.0; 95%CI: 4.33-299.09; P = 0.0009).

CONCLUSION: Small isolated whitish round area by NM-NBI endoscopy is a useful finding of SRCs which is the indication for ESD.

Key words: Gastric cancer; Signet ring cell carcinoma; Narrow-band imaging; Intramucosal cancer; Endoscopic submucosal dissection

Core tip: Intramucosal signet ring cell carcinoma (SRC) $\leqslant$ 2 cm in diameter, for which endoscopic submucosal dissection is indicated, is very difficult to identify by white-light imaging (WLI) endoscopy. However, little is known regarding non-magnifying narrow-band imaging (NM-NBI) findings of early SRC. The strength and shape of the SRCs by NM-NBI and WLI were assessed with Image J. NM-NBI findings of SRC showed a clearly isolated whitish area amid the brown color of the surrounding normal mucosa. The NBI index, which indicates the potency of NBI for visualizing SRC, was significantly higher than the WLI index (P = 0.001).

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INTRODUCTION

Gastric cancer ranks as the fourth most common cancer and the second most frequent cause of death from cancer in the world[1]. *Helicobacter pylori* (*H. pylori*) infection is considered to be a main risk factor for the development of gastric cancer of either intestinal or diffuse type[2]. However, according to recent reports, the *H. pylori* infection rate has decreased over the last 40-50 years in both Asia and Western countries, with an overall decline in *H. pylori* seroprevalence[3,4]. In Japan, the prevalence of *H. pylori*-negative gastric cancer is extremely low; therefore, the prevalence of gastric cancer may continue to decrease substantially as the *H. pylori* infection rate continues to decrease[5,6]. The pathological characteristics of *H. pylori*-negative gastric cancer are different from those of *H. pylori*-positive gastric cancer; histologically, the diffuse type is dominant, especially signet ring cell carcinoma (SRC) (60%)[6]. Commonly, SRC of the stomach is thought to arise in the mucosa without metaplastic change and is typically confined to the glandular neck region in the original proliferation zone[7]. It is considered, therefore, that early-stage SRCs can be present beneath a flat, intact mucosal surface epithelium, and may be very difficult to identify by white-light imaging (WLI) endoscopy due to their slightly whitish discoloration.

Recently, magnifying narrow-band imaging (NBI) has been reported to be useful for the accurate diagnosis of gastric cancers, even for small, depressed gastric mucosal cancers[8-11]. Several studies have demonstrated an association between the histology, *i.e.*, differentiated *vs* undifferentiated type, and magnified NBI appearance[8,11-13]. In cases of SRC, the cancer-specific findings and identifiable demarcation line of the lesion may not be identified even by magnifying NBI endoscopy or chromoendoscopy[12,13]. We have found intramucosal SRCs by non-magnifying NBI (NM-NBI) endoscopy that we failed to detect by WLI endoscopy. Nonetheless, there has been little research into NM-NBI findings focused strictly on intramucosal SRCs.

It has been reported that patients with SRC caught at an early stage can expect a better prognosis than they might with other gastric cancers[14] and SRC is not a prognostic factor in early cancer[15]. The prognosis of those at the advanced stage is still controversial; a report by Otsuji *et al*[14] from Japan showed no significant difference in 5-year survival rates between patients with SRC and those with other histological types of gastric cancer, while other studies from the West[16-18] have found that SRC has a worse prognosis due to specific characteristics such as high rate of lymph node metastasis and peritoneal carcinomatosis. Clearly, it is best to discover gastric SRC early, but the early detection of lesions located beneath a preserved surface epithelium may be very difficult.

Although NBI is increasingly available in endoscopy units, only a limited number of cases are subjected to magnifying NBI endoscopy, even in hospitals specializing in gastroenterology. Many gastroenterologists or endoscopists use a conventional NM-NBI endoscope lacking a magnification function to screen for gastric cancer. In the present study, we (1) retrospectively investigated endoscopic findings of SRC by NM-NBI endoscopy and WLI endoscopy; and (2) compared the NBI findings of SRC and whitish gastric ulcer scars, in order to clarify the NM-NBI features of SRC.

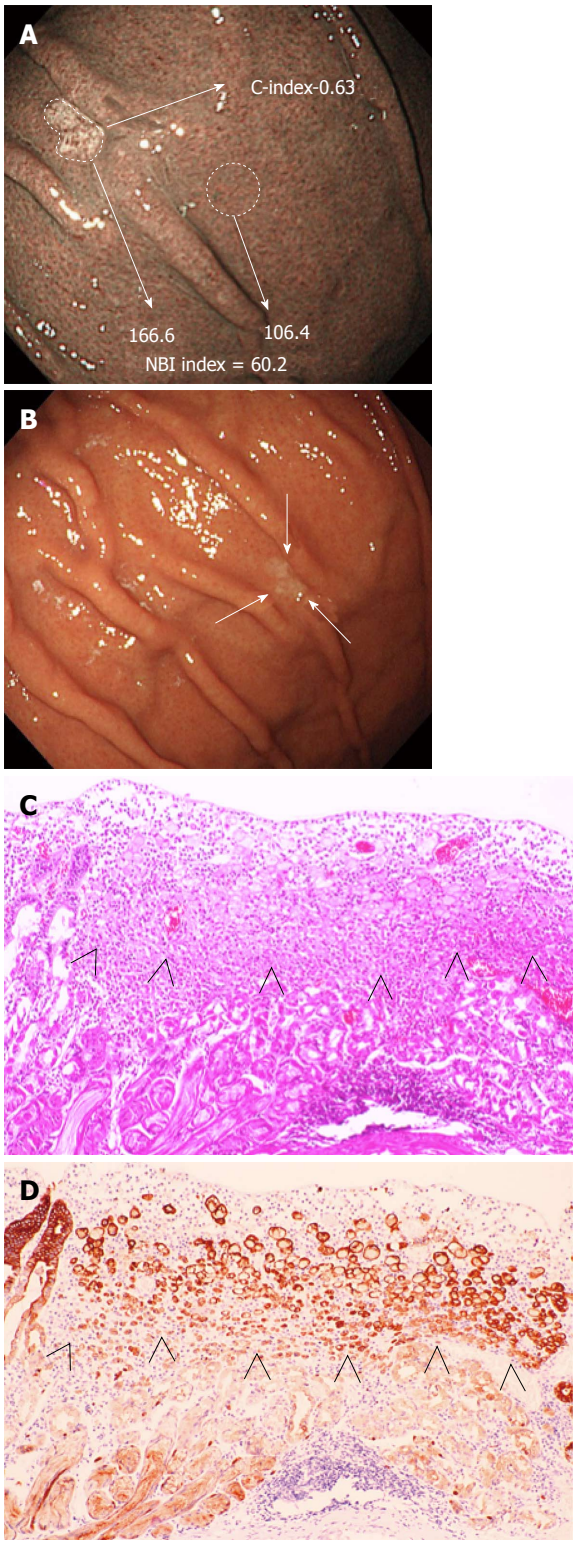

Figure 1 Endoscopic and histologic findings of signet ring cell carcinomas localized at the greater curvature of the corpus (Case 4). A: NBI of the cancer area showed an isolated oval-shaped whitish area. The NBI index was 60.2. The C-index was 0.63; B: Endoscopy with WLI showed a 0-IIc lesion with slight discoloration (arrows) at the greater curvature of the corpus. The WLI index was 4.5; C: The histology by endoscopic submucosal dissection showed an intramucosal SRC in the upper third of the gastric mucosa (arrowheads) with a partial defect of the foveolar epithelium; D: Immunohistochemical staining of SRC cells showed diffuse positive reactivity for cytokeratin AE1/AE3 (arrowheads). NBI: Narrow-band imaging; WLI: White-light imaging; SRC: Signet ring cell carcinoma.

MATERIALS AND METHODS

Patients

Between January 2011 and May 2014 in our department, 322 early gastric cancers or adenomas in 301 patients were treated with endoscopic submucosal dissection (ESD). The indications for ESD of intramucosal gastric cancer or adenoma, included the following[19]: (1) intramucosal differentiated-type adenocarcinoma of any size without ulceration; (2) intramucosal differentiated-type adenocarcinoma with an ulcer scar and measuring $\leqslant$ 3 cm in diameter; and (3) intramucosal undifferentiated-type adenocarcinoma, including poorly differentiated cancer or SRC, of less than 2 cm without an ulcer scar. In all cases, the histology, tumor location, macroscopic classification, and depth of invasion fulfilled the criteria of the Japanese Research Society for Gastric Cancer[20]. Among these cases treated with ESD, 14 (4.3%) were diagnosed histologically as intramucosal SRC ($\leqslant$ 2 cm) without any other findings of adenocarcinoma. During the same period, 14 patients with whitish gastric ulcer scars that were histologically confirmed by biopsy were randomly selected as controls.

Methods

Written informed consent was obtained from all patients who underwent a routine endoscopic examination and ESD, and this study was conducted in accordance with the guidelines of the Declaration of Helsinki. All patients underwent NM-NBI endoscopy by an endoscope (GIF-Q260) or high-vision endoscope (H260, H260Z, H290 and HQ290) with an electronic endoscopic system (Evis Lucera CV-260 SL or Elite CV-290; Olympus Medical Systems, Corp., Tokyo, Japan). The strengths of the NM-NBI and WLI images of 14 consecutive gastric SRCs undergoing ESD and the strength of the NM-NBI images of gastric ulcer scars (controls) were quantified with an image-analytical software program. Briefly, NBI images were converted into joint photographic experts group pictures; then the cancer or ulcer scar area on the pictures was manually traced with an image-analytical software program (ImageJ ver. 1.48; National Institutes of Health, Bethesda, MD). Using the default tool "Measure" under the "Analyze" menu, the mean gray value (MGV) of the cancer or ulcer area was calculated, and the MGV of a region of similar area of the perilesional normal mucosa was also measured. The MGV of the cancer or ulcer scar area minus that of the perilesional area was defined as the NBI index (Figure 1; note, a brighter image has a higher MGV). In addition, the values for several shape descriptors of the SRCs and gastric ulcer scars were also calculated to assess their shapes. Briefly, using the default tool "Measure" under the "Analyze" menu, "Circ." was adopted as the circularity index (C-index). The C-index value of a perfect circle is 1; as the shape deviates from perfectly circular, the C-index value decreases (Figure 2). The WLI strength was calculated as well as the NM-

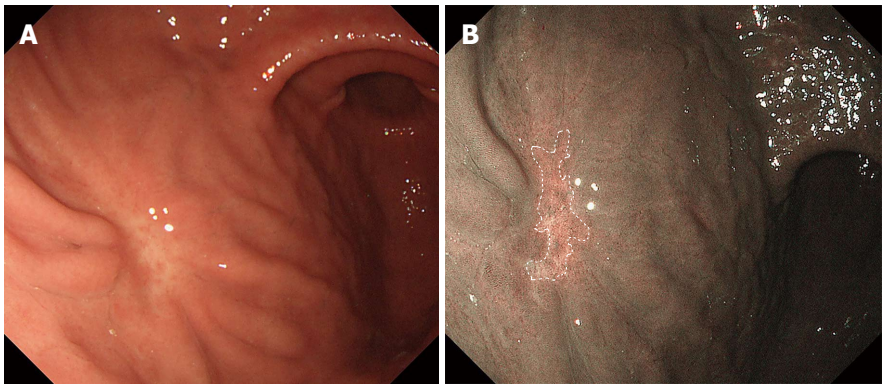

Figure 2 Endoscopic images of whitish gastric ulcer scars. White-light imaging (A) and non-magnifying narrow-band imaging (B). The NBI index and C-index were 44.9 and 0.29, respectively. NBI: Narrow-band imaging; C-index: Circularity index.

Table 1 Characteristics of signet ring cell carcinoma patients and controls

	SRC	Control	*P* value
Age, yr, mean ± SD	53.2 ± 14.2	69.1 ± 14.8	0.0008
Sex, male/female	7/6	10/4	0.44
Location: upper/middle/lower	2/7/5	4/8/2	0.36
NBI finding			
NBI index (mean ± SD)	27.9 ± 21.0[a]	24.8 ± 14.7	0.78
H. pylori: positive/negative	26.1 ± 20.5/29.0 ± 22.4	27.8 ± 15.4/19.3 ± 13.2	0.95 in SRC and 0.26 in control
WLI finding (mean ± SD)			
WLI index	5.3 ± 16.2[a]	-	0.001[a]
H. pylori: positive/negative	13.5 ± 16.4/0.7 ± 15.1	-	0.32
C-index (mean ± SD)	0.67 ± 0.13	0.50 ± 0.14	0.001

[a]*P* = 0.001 between NBI index and WLI index. SRC: Signet ring cell carcinoma; NBI: Narrow-band imaging; WLI: White light imaging; C-index: Circularity index.

NBI index, and was measured by "RGB Measure (R + G + B/3)" tool under the "Analyze" menu in "Plugins". The quantification was performed by an endoscopist who was not involved in the patients' original diagnoses or treatments.

To assess *H. pylori* infection, biopsy specimens, two from each site, were taken from the greater curvature of the antrum and body of the stomach. *H. pylori* status was analyzed in each patient by two methods: Giemsa staining and serum *H. pylori*-IgG antibody with an enzyme-linked immunosorbent assay kit using the E plate test (Eiken Kagaku, Tokyo, Japan). A patient was regarded as positive for *H. pylori* if at least one of these tests was positive.

Statistical analysis

The data were assessed by the Mann-Whitney *U*-test for comparisons between two independent groups and the Fisher's exact test for comparisons between two proportions. NM-NBI findings including the NBI-index and C-index were included as potential malignant features for SRC in univariate analysis. Multivariate logistic regression analyses were performed to identify significant predictive NBI findings. Odds ratios and 95%CIs were used to assess the statistical significance at the conventional level of 0.05. Statistical analysis was performed with StatView version 5.0 (SAS Institute Inc., Cary, NC). Receiver operating characteristic (ROC) curve was calculated for the highest diagnostic performance in terms of the shape of SRCs (C-index), and then the curve was plotted using JMP 10 software (SAS Institute Inc., Cary, NC). The area under the ROC curve and the optimal thresholds using the Youden index were calculated from ROC analysis[21].

RESULTS

Table 1 shows the characteristics of the 14 SRCs in the 13 patients who underwent ESD and the controls. In addition, clinical and endoscopic data of SRCs are shown in Table 2. Out of 14 SRCs, 10 lesions were detected at other hospitals and then referred to our department for ESD treatment. Two (cases 4 and 12) of the 14 SRCs were first identified by NM-NBI endoscopy, but not by WLI endoscopy, in our department (Figure 1). In SRC patients, the mean age was 53.2 ± 14.2 years (range: 23 to 74 years), and women accounted for 46.2% (6 of 13) of the group. In contrast, the mean age of the controls was 69.1 ± 14.8 years, significantly higher than that of the SRC patients. The *H. pylori*-negative rate was 69.2% (9 of 13) in the SRC patients, and none of these patients had received *H. pylori* eradication therapy. In the control group, 4 out of 5 *H. pylori*-negative patients (35.7%, 5 of 14) had undergone eradication

Table 2 Characteristics of signet ring cell carcinomas in the 13 patients

Case	Age	Sex	Type	Size (mm)	Location	Location	*Hp*	PDE	NBI index	WLI index	C-index	Endoscopic system
1	23	Female	Ⅱb	4	M	GC	+	-	22.5	3.5	0.75	CV-260 SL
			Ⅱc	6	L	GC		-	25.6	16.1	0.67	CV-290
2	63	Female	Ⅱb	14	M	LC	+	+	5.5	2.2	0.76	CV-260 SL
3	62	Male	Ⅱc	15	M	GC	+	-	16.8	41.1	0.61	CV-260 SL
4	74	Female	Ⅱc	4	U	GC	+	+	60.2	4.5	0.63	CV-260 SL
5	48	Male	Ⅱc	4	L	GC	-	-	59.6	0.22	0.66	CV-260 SL
6	62	Male	Ⅱb	5	M	LC	-	+	17.6	-2.7	0.81	CV-260 SL
7	48	Male	Ⅱc	2	U	GC	-	-	1.0	4.0	0.33	CV-260 SL
8	58	Male	Ⅱc	5	L	LC	-	-	19.5	-33.7	0.88	CV-260 SL
9	40	Female	Ⅱb	6	M	GC	-	-	25.6	12.8	0.77	CV-290
10	69	Female	Ⅱb	8	L	PW	-	-	68.5	-8.5	0.60	CV-290
11	46	Male	Ⅱb	5	M	GC	-	-	10.8	9.3	0.63	CV-290
12	60	Male	Ⅱb	6	M	GC	-	-	19.7	16.3	0.57	CV-290
13	38	Female	Ⅱb	6	L	PW	-	-	38.2	8.7	0.69	CV-290

Hp: *Helicobacter pylori*; PDE: Partially defect of epithelium; L: Lower third of the stomach; M: Middle third of the stomach; U: Upper third of the stomach; GC: Greater curvature; LC: Lesser curvature; PW: Posterior wall; C-index: Circularity index; NBI: Narrow-band imaging; WLI: White light imaging.

therapy previously.

Most SRCs were located in the middle or lower portion of the stomach (85.7%, 12 of 14) and at the greater curvature (64.3%, 9 of 14), with no significant difference in the distribution of lesions compared to the control. The average diameter of the major axis of the SRCs was 6.4 mm (range: 2 to 15 mm). Histologically, a partial defect of the foveolar epithelium was identified in only 3 cases (21.4%); thus, most SRC cells were found beneath a preserved surface epithelium. In all SRC cases, the histological growth pattern of cancer cells corresponded to the non-whole-layer type according to the definition by Okada *et al*[13].

NM-NBI and WLI findings

In SRCs, NBI findings showed a clearly isolated whitish area amid the brown color of the normal mucosa. The NBI index (27.9 ± 21.0) was significantly higher than the WLI index (5.3 ± 16.2) (P = 0.001), indicating that the contrast between the cancer and surrounding normal mucosa was more intense by NM-NBI than by WLI. This result indicates that the cancerous areas were more clearly captured by NM-NBI endoscopy than by WLI endoscopy (Figures 1 and 3). The overall mean NBI index was 27.9 ± 21.0; this value was not significantly different from that (24.8 ± 14.7) of the control. Moreover, the NBI indices were not significantly different between the *H. pylori*-positive and -negative cases in either the SRCs or controls. In addition, the WLI index of the SRCs was not significantly different between *H. pylori*-positive and -negative cases. In contrast, the C-index was significantly higher in SRCs (0.67 ± 0.13) than in controls (0.50 ± 0.14) (P = 0.001), indicating that SRCs are rounder in shape than ulcer scars (Table 1). The C-index was the only factor significantly associated with SRCs in the NBI findings.

Association between the shape of SRCs and C-index

The association between the shape of SRCs and C-index was evaluated using ROC curve analysis (Figure 4). According to this analysis, the resulting cut-off value of the C-index for SRC was 0.60 (sensitivity, 85.7%; specificity, 85.7%).

Based on the ROC curve analysis and optimal cut-off points of the C-index of SRC determined above, a C-index of ⩾ 0.60 was used in the analysis. We investigated the strength of the association between the C-index (⩾ 0.60) in the NM-NBI findings and that in the SRCs by means of a logistic regression analysis. The C-index (⩾ 0.60) was found to be a significant predictor of SRCs (OR = 36.0; 95%CI: 4.33-299.09; P = 0.0009).

DISCUSSION

As the *H. pylori* infection rate continues to decrease, cardiac or junctional gastric cancer and histologically undifferentiated-type adenocarcinoma including SRC will increase in proportion. Therefore, there is need of an easy method for detecting these cancers in an early stage by routine endoscopy. Magnifying NBI is definitely useful for the accurate diagnosis of gastric cancer or dysplasia using the criteria for gastric cancer: irregularity or disappearance of the mucosal structure or a microvascular pattern in a definite demarcation line[8-13]. However, small intramucosal SRCs (⩽ 2 cm), which are best treated by ESD, have fewer of these magnifying NBI findings, because most intramucosal SRC cells are covered by a normal foveolar epithelium. To the best of our knowledge, this is the first study to report on the NM-NBI findings and clinical features of small SRC, for which endoscopic treatment is indicated.

In a previous magnifying NBI study of undifferentiated-type early gastric cancer including SRCs[8,11-13], Okada *et al*[13] found that gastric cancers with a preserved but irregular surface pattern corresponded histologically to the non-whole-layer type of mucosal cancer, whereas cancers with an irregular microvascular pattern or mixed pattern upon magnifying NBI corresponded histopathologically to the whole-layer type of intramucosal cancer or submucosal invasion

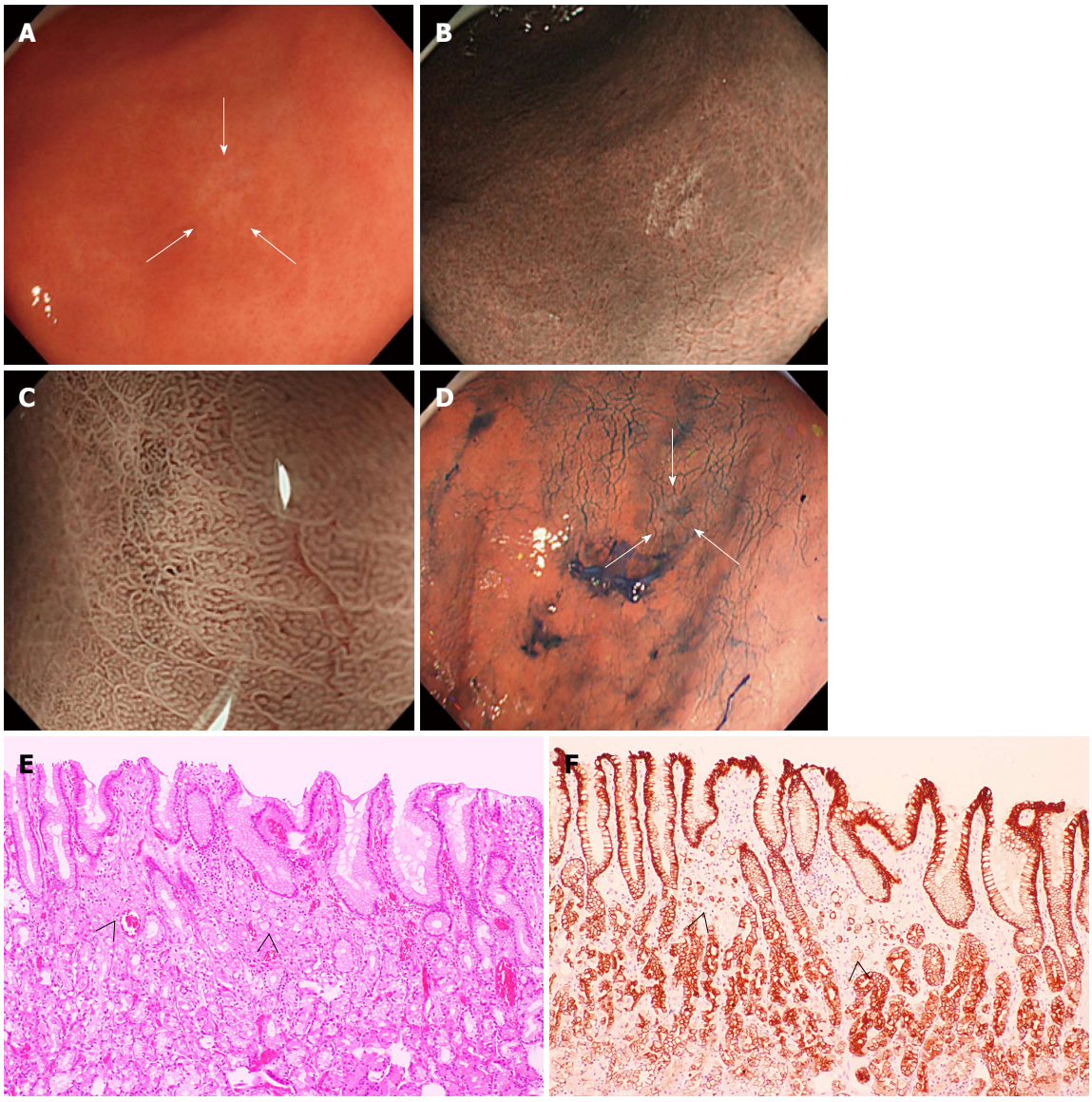

Figure 3 Endoscopic and microscopic images of signet ring cell carcinoma (Case 9). A: Endoscopy with WLI revealed a 0-IIb lesion with slight discoloration (arrows) at the greater curvature of the angulus; B: NM-NBI of the cancer area showed an isolated clear whitish area. The cancerous areas were more clearly captured by NM-NBI endoscopy than by WLI endoscopy. The NBI and WLI index were respectively 25.6 and 12.8, and the C-index was 0.77; C and D: The demarcation line of the SRC was not clearly identified even by magnifying NBI and chromoendoscopy (arrows); E: The histology of a specimen resected by endoscopic submucosal dissection revealed an intramucosal SRC (arrowheads) in the upper third of the mucosa beneath a preserved surface epithelium; F: SRC cells showed positive for cytokeratin AE1/AE3 staining (arrowheads). WLI: White-light imaging; NM-NBI: Non-magnifying narrow-band imaging; SRC: Signet ring cell carcinoma.

cancer[13]. In cases of small undifferentiated-type cancer in which cells infiltrate laterally in the lamina propria deep into the glandular neck, *i.e.*, the non-whole-layer type, magnifying NBI cannot detect any cancer-specific irregular microvascular or microsurface pattern[9]. Therefore, it is difficult to detect undifferentiated-type cancer developing laterally within the proliferative zone and to identify the demarcation line of the cancer even by magnifying NBI, as shown in Figure 3[13]. Moreover, the extent of the lateral margin in this type of cancer becomes less detectable by chromoendoscopy (Figure 3)[12].

In the current study, however, SRCs were captured more easily by NM-NBI without the use of a magnifying endoscope than by WLI endoscopy; on NM-NBI they appeared as isolated whitish round areas. It remains unclear why the cancerous area of the SRC is whitish when compared to the surrounding normal mucosa. One possibility is that the depth of the crypt is shallow and the surface of the mucosa is planarized because of closely aggregated SRC cells in the upper to middle third of the mucosa (Figures 1 and 3). Okada *et al*[13] similarly presumed that both the number and heights of the gastric pits were decreased due to the extension of cancer cells in the mucosa, which eventually obliterated the architecture of the microsurface. As *H. pylori* infection causes extensive infiltration of inflammatory cells into the gastric mucosa, one would think this inflammation might affect the NBI index. However, no significant difference in the NBI index was seen

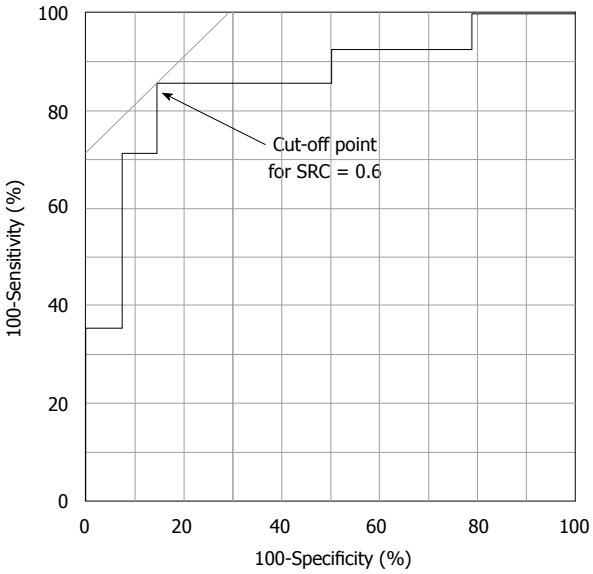

Figure 4 Receiver operating characteristic curve of the C-index of signet ring cell carcinoma. The curve is plotted as sensitivity (Y axis) and (100-specificity) (X axis). SRC: Signet ring cell carcinoma.

between patients with and without *H. pylori* infection in either SRCs or controls. There was also no significant difference in the NBI index between the SRC and control groups themselves, while the C-index results indicated that the SRCs were significantly rounder than the gastric ulcer scars of the controls. Since the 1980s, irregular shape lesion has been known to reflect malignant finding in the diagnosis of small gastric cancers, especially those of differentiated-type[22], and thus the NM-NBI shape of small SRC might be different from that of differentiated-type cancer. In the present work, a C-index exceeding 0.60 was considered to be the most reliable factor associated with SRCs. In logistic regression analysis, as well, the C-index ($\geqslant$ 0.60) was a highly significant predictor for SRC (OR = 36.0; 95%CI: 4.33-299.09; P = 0.0009). These results may suggest that NM-NBI could easily discriminate SRCs from gastric ulcer scars. However, gastric ulcer scars are histologically associated with complicated fibrosis in the submucosal layer, and thus it may not be surprising that their shape tended to be more irregular than that of SRCs.

More recently, novel electronic endoscopic systems (Evis Lucera Elite CV-290 and LASEREO, FUJIFILM Medical Co., Ltd., Tokyo) have been newly developed. These systems enable clearer and brighter NBI observation throughout the entire stomach than the existing systems (Evis Lucera CV-260 SL and Advancia, FUJIFILM Medical Co., Ltd., Tokyo). Therefore, it may be possible to identify small SRCs even from a relative distance by using a novel electronic endoscopic system. SRCs may be a form of incipient gastric cancer that may eventually develop into a linitis plastica-type cancer; hence, it is important to detect SRCs at an early stage. Our findings suggest the need to look carefully for isolated whitish round areas on NBI endoscopy, particularly in the greater curvature of the middle to lower portion of the stomach.

Nevertheless, the present study had some potential limitations. First, this was a retrospective study from a single institution with a small number of SRC cases. It will be important to perform a prospective study using the NBI criteria in order to confirm the reliability of these findings. However, the incidence of intramucosal SRC is low (4.3%) among the cases treated with ESD. Therefore, the incidence will be even lower in patients who undergo endoscopy for screening, indicating that a larger series of samples and an appreciable length of time will be required to assess the reliability. Second, ten of the SRC cases were referred to our department after biopsies at other clinics or hospitals; most lesions were biopsied prior to imaging. Thus, previous biopsy sites were covered by regenerated epithelium and might have influenced the NM-NBI findings[13]. However, the NBI index was not significantly different between biopsied and non-biopsied cases (data not shown).

In conclusion, it is best to look carefully for isolated whitish round areas by NM-NBI endoscopy for early detection of this malignancy. Here, we would like to emphasize that during an era when the incidence of *H. pylori* infection is decreasing, NM-NBI endoscopy should be used for the detection of small intramucosal SRCs.

COMMENTS

Background

As the authors described, the pathological characteristics of *Helicobacter pylori* (*H. pylori*)-negative gastric cancer are different from those of *H. pylori*-positive gastric cancer; histologically, the diffuse type is dominant, especially signet ring cell carcinoma (SRC). Since early-stage SRC develops beneath a flat, intact mucosal surface epithelium, it is very difficult to identify by white-light imaging (WLI) endoscopy.

Research frontiers

Magnifying narrow-band imaging (NBI) has been reported to be useful for the accurate diagnosis even in small gastric mucosal cancers. In cases of SRC, however, the cancer-specific findings and identifiable demarcation line of the lesion may not be identified even by magnifying NBI endoscopy or chromoendoscopy. To date, little is known regarding non-magnifying (NM)-NBI findings of small intramucosal SRC.

Innovations and breakthroughs

Intramucosal SRC could be clearly captured by NM-NBI as an isolated whitish area amid the brown color of the surrounding normal mucosa. SRCs were more clearly captured by NM-NBI endoscopy than by WLI endoscopy. Furthermore, although the NBI strengths of SRCs and whitish gastric ulcer scars were not significantly different, the two types of lesions' indexes of circularity determined by image-analytical software were significantly different, with the SRCs being distinctly rounder in shape than the ulcer scars.

Applications

This study emphasizes that during an era when the incidence of *H. pylori* infection is decreasing, NM-NBI endoscopy should be used for the detection of small intramucosal SRCs, which is indicated for endoscopic submucosal dissection. It is best to look carefully for isolated whitish round areas by NM-NBI endoscopy for early detection of this malignancy.

Terminology

NBI: Magnifying endoscopy with NBI is widely used in gastroscopy, especially in

the diagnosis of early gastric cancer. SRC: Signet ring cell carcinoma is thought to arise in the mucosa without metaplastic change and is typically confined to the glandular neck region in the original proliferation zone; therefore, it is difficult to detect those lesions.

Peer-review

The manuscript is excellent with perfect language.

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DOI: 10.4253/wjge.v7.i12.1078

World J Gastrointest Endosc 2015 September 10; 7(12): 1078-1082
ISSN 1948-5190 (online)

ORIGINAL ARTICLE

Clinical Trials Study

Laparoscopic right-sided colonic resection with transluminal colonoscopic specimen extraction

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Author contributions: Kayaalp C designed research; Kayaalp C, Kutluturk K, Yagci MA, Ates M performed research; Kayaalp C contributed to new reagents or analytic tools; Kayaalp C and Yagci MA analyzed data; Kayaalp C and Kutluturk K wrote the paper.

Institutional review board statement: The study was reviewed and approved by Inonu University Institutional Review Board.

Clinical trial registration statement: This study is registered at Inonu University Human Ethical Committee as a research. The registration identification number is 2014/33.

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

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

Data sharing statement: No additional data are available.

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Received: September 18, 2014
Peer-review started: September 18, 2014
First decision: December 17, 2014
Revised: June 9, 2015
Accepted: July 7, 2015
Article in press: August 24, 2015
Published online: September 10, 2015

Abstract

AIM: To study the transcolonic extraction of the proximally resected colonic specimens by colonoscopic assistance at laparoscopic colonic surgery.

METHODS: The diagnoses of our patients were Crohn's disease, carcinoid of appendix and adenocarcinoma of cecum. We preferred laparoscopic total mesocolic resections. Colon and terminal ileum were divided with endoscopic staplers. A colonoscope was placed per anal and moved proximally in the colon till to reach the colonic closed end under the laparoscopic guidance. The stump of the colon was opened with laparoscopic scissors. A snare of colonoscope was released and the intraperitoneal complete free colonic specimen was grasped. Specimen was moved in to the colon with the help of the laparoscopic graspers and pulled gently through the large bowel and extracted through the anus. The open end of the colon was closed again and the ileal limb and the colon were anastomosed intracorporeally with a 60-mm laparoscopic stapler. The common enterotomy orifice was closed in two layers with a running intracorporeal suture.

RESULTS: There were three patients with laparoscopic right-sided colonic resections and their specimens were intended to remove through the remnant colon by colonoscopy but the procedure failed in one patient (adenocarcinoma) due to a bulky mass and the specimen extraction was converted to transvaginal route. All the patients had prior abdominal surgeries and had related adhesions. The operating times were 210, 300 and 500 min. The lengths of the specimens

were 13, 17 and 27 cm. In our cases, there were no superficial or deep surgical site infections or any other complications. The patients were discharged uneventfully within 4-5 d and they were asymptomatic after a mean 7.6 mo follow-up (ranged 4-12). As far as we know, there were only 12 cases reported yet on transcolonic extraction of the proximal colonic specimens by colonoscopic assistance after laparoscopic resections. With our cases, success rate of the overall experience in the literature was 80% (12/15) in selected cases.

CONCLUSION: Transcolonic specimen extraction for right-sided colonic resection is feasible in selected patients. Both natural orifice surgery and intracorporeal anastomosis avoids mini-laparotomy for specimen extraction or anastomosis.

Key words: Colonoscopy; Colon cancer; Crohn's disease; Laparoscopic surgery; Natural orifice transendoscopic surger; Natural orifice specimen extraction

Core tip: Transcolonic extraction of the proximally resected colonic specimens by colonoscopic assistance can be an attractive method for some selected cases. This technique requires both advanced laparoscopic experience by intracorporeal anastomosis and interventional endoscopy. In this technique, there was a far distance between the resected specimen and the natural orifice. The specimen is moved about 100 cm in a hollow organ till the natural orifice. As far as we know, it has been the farthest distance that was reported yet for natural orifice specimen extractions. However, this technique is only suitable for small specimens which can pass through the sigmoid colon.

Kayaalp C, Kutluturk K, Yagci MA, Ates M. Laparoscopic right-sided colonic resection with transluminal colonoscopic specimen extraction. *World J Gastrointest Endosc* 2015; 7(12): 1078-1082 Available from: URL: http://www.wjgnet.com/1948-5190/full/v7/i12/1078.htm DOI: http://dx.doi.org/10.4253/wjge.v7.i12.1078

INTRODUCTION

Laparoscopic colectomy is going on to increase the number of its supporters. It lets smaller abdominal incisions and this reflects several advantages such as less pain, rapid recovery and wound problems. However, the required mini-laparotomy to extract the specimen during laparoscopic colectomy clearly compromise some advantages of the laparoscopic surgery. The use of natural orifices such as vagina or anus for colonic extraction is a new concept and it can avoid this mini-laparotomy and related morbidities. This new concept is called as Natural Orifice Specimen Extraction (NOSE) and the first laparoscopic colectomy with transanal specimen extraction has been described at the beginning of 1990's[1]. Up to the present time, transanal extraction was the main route for the rectal and left sided colonic specimens and transvaginal route was also available for both left and right sided colonic resections[1]. Transcolonic extraction by colonoscopic assistance can be an attractive method for some selected right-sided colonic resections but, as far as we know, there are only 12 cases reported yet[2-4]. Here, we reported three more patients with laparoscopic right-sided colonic resections and their specimens were intended to remove transanally by colonoscopy. The aim of this study was (1) to describe our initial clinical experience; (2) to outline our differences from the previous reports; and (3) to review all the available published cases.

MATERIALS AND METHODS

Mechanical bowel preparation was given the night before surgery. Broad-spectrum intravenous antibiotics were administered 30 min before skin incision and postoperatively for three days. Following induction of general anesthesia, a urinary catheter and a nasogastric tube were inserted. The patient were placed in the modified lithotomy position, with legs abducted and slightly flexed at the knees. The abdomen was insufflated by Veress and total of three or four abdominal trocars were used (two 5-12 mm and one or two 5 mm trocars) (Figure 1). The patient was placed in a 15 degree right-up lateral position. We preferred total mesocolic resections for all patients. Medial to lateral mesenteric dissection was carried out and when we identified the distal resection margin, we created a window in the mesocolon at this level and we divided the colon with a 60 mm endoscopic stapling device (EndoGIA, Covidien, Mansfield, MA). The lateral peritoneal attachments of the colon were mobilized from top-to-bottom until the cecum and terminal ileum was transected using the same endoscopic 60-mm linear stapler. A colonoscope was placed per anal and moved proximally in the colon till to reach the colonic closed end under the laparoscopic guidance. Laparoscopically, the stump of the colon was opened with endoscopic scissors and the colonoscope was visualized in the colon (Figure 2). A snare of colonoscope was released and the intraperitoneal complete free colonic specimen was grasped (Figure 3). Specimen was moved in to the colon with the help of the endoscopic graspers and pulled gently through the large bowel by colonoscope. If there was any invagination, it was reduced with graspers. The specimen was pulled through the remnant colon under laparoscopic guidance and extracted through the anus. The open end of colon was closed again with a laparoscopic stapler and the tiny remnant of colonic specimen removed through the 12 mm trocar. The ileal limb and the colon were anastomosed intracorporeally with a 60-mm laparoscopic stapler. The common enterotomy orifice was closed in two layers with a

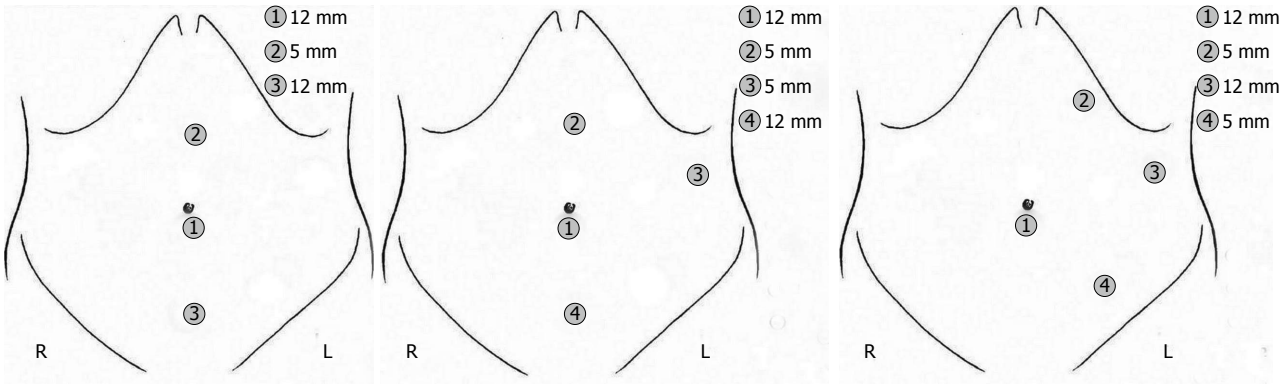

Figure 1 Trocar placements of the patients.

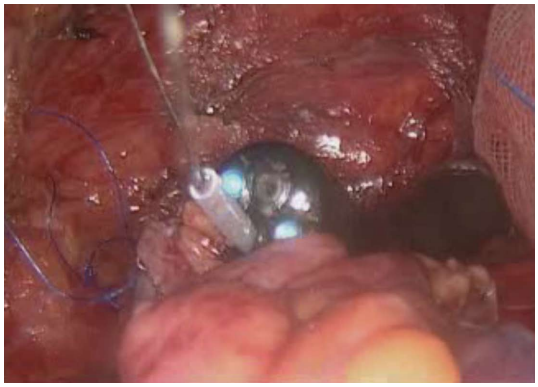

Figure 2 Intraperitoneal view of the colonoscope passed through the rectum, left colon and transverse colon. It is ready to grasp the laparoscopically resected right colon that was completely free in the abdomen.

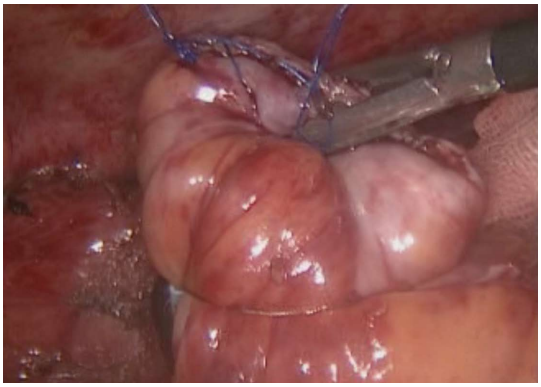

Figure 3 Colonoscopic transcolonic removal of the right colonic specimen.

running intracorporeal suture. An abdominal drain was placed. The nasogastric tube was removed at the end of the operation.

RESULTS

All the details of the patients, diseases and surgical procedures were summarized in Table 1. First patient had a Crohn's disease with intermittent bowel obstruction. He had a previous open appendectomy. Radiologically confirmed ileocolic stenosis was treated by laparoscopic ileocolic resection. There were bulky mesenteric lymph nodes which were very close to the stenotic part of the bowel. Bulky specimen caused some difficulties during transcolonic extraction and the specimen moved in the sigmoid colon in difficulty but the procedure was completed successfully without any complication. The second patient had a history of open appendectomy three months ago. The pathology reported carcinoid tumor with perineural invasion. A laparoscopic right hemi-colectomy with colonoscopy assisted transluminal specimen extraction was performed. There was no problem during transcolonic transit and extraction of the specimen. Pathological examination showed no malignancy. Last patient had a previous history of open pancreaticoduodenectomy due to chronic pancreatitis. While she was investigated for anemia, a 5-cm ulcerous cecal adenocarcinoma was detected. After laparoscopic right hemi-colectomy the specimen was tried to extract through the transcolonic route but it failed due to the bulky tumor and lymph nodes. In this case, we worried about jamming the specimen in the colon and it was removed from the vagina. The pathological analysis showed a pT3pN2 adenocarcinoma. None of the patients had early or late complication after a mean 7.6 mo (ranged 4-12) follow-up (Table 1).

DISCUSSION

Here, we intended to do a more minimal invasive colorectal surgery than the conventional laparoscopic technique and described three more cases of transcolonic extraction route for right-sided colonic pathologies. The potential advantages of natural orifice surgery are lower risks of incision related complications such as wound infections, postoperative pain, incisional hernias and better cosmesis. None of our cases had wound related early (surgical site infection) or late complication (hernia) in their follow-up. Because all our patients had previous open abdominal surgeries, there were no clear advantage of cosmesis. On the other hand, we learnt that previous abdominal surgery was not an obstacle for transcolonic specimen extraction.

Table 1 Published right hemicolectomies that the specimens were removed through the colon

	Patient No. 1	Patient No. 2	Patient No. 3	Eshuis[1] (*n* = 10)	Saad (*n* = 1)	Takayama (*n* = 1)
Age (yr)	55	20	68	31 (19-61)	70	71
Gender	M	F	F	3 M, 7 F	F	M
BMI	22	20	27	23.7 (18-31)	NA	NA
ASA	II	I	II	NA	NA	NA
Previous surgery	Yes	Yes	Yes	NA	NA	NA
Operating time (min)	210	300	500	208 (157-327)	NA	240
Blood loss (mL)	20	< 10	400	NA	NA	28
Specimen length (cm)	13	17	27	25.5 (16-64)	NA	8
Specimen width (cm)	8	6	12	> 7 cm (*n* = 2) < 7 cm (*n* = 8)	NA	NA
Failure	No	No	Yes	Yes (*n* = 2)	No	No
Complications	No	No	No	Yes (*n* = 3)	No	No
Resection location	Ileocolic	RHC	RHC	Ileocolic	Transverse	Ileocolic
Pathology	Crohn's	Carcinoid	Cancer	Crohn's	Adenoma	Adenoma
Oral diet (d)	3	3	2	NA	NA	1
Hospital stay (d)	5	5	4	5 (2-10)	5	4
Follow-up (mo)	12	7	4	NA	NA	NA

[1]Numbers of Eshuis are median and range in parenthesis. ASA: American Society of Anaesthesiologists physical status classification; NA: Not available; M: Male; F: Female; BMI: Body mass index.

There are two natural orifices for colorectal specimen extraction: the vagina and the anus. Transvaginal extraction can have some pitfalls. It is limited to female patients, requires an additional surgical trauma to an innocent organ and is not always suitable for patients of childbearing age, teenagers and virgins. Our second case was a virgin and she refused transvaginal access. She specified a preference for transabdominal extraction if the transcolonic extraction failed during surgery. The transanal route is more natural for colorectal specimen extractions and it can be considered as the first option for left sided colorectal resections[1] or total colectomies[5]. The transvaginal route can be kept particularly for bulky right sided colonic resections which are not suitable for transcolonic extraction. We preferred the transvaginal route for one case in which the transcolonic extraction failed due to a bulky specimen.

There is no clear description for the limitations of transcolonic specimen extraction. Splenic flexura of the colon (kinking) and the sigmoid colon (narrowing) are the two natural barriers during the transcolonic removal. It is a rational method to select the specimen sizes according to those natural narrow or kinking passes. After extractions, we measured the largest width of the specimens and they were 8, 6 and 12 cm (failed case), respectively. Although the largest width of the specimen is an important parameter, we believe that the largest diameter of the rolled specimen is more important. Eshuis *et al*[2] advocated performing transcolonic extraction of specimens with a maximum diameter of 5 cm in patients without inflammatory masses. They aborted two of ten cases due bulky volumes. It is not easy to estimate the largest diameter of every specimen by preoperative evaluation. Moreover, large masses at scans sometimes can be suitable for natural extraction and contrary, the procedure can fail for some small-looking lesions. Therefore we suggest intraoperative evaluation for decision. We decided to remove two specimens by transcolonic way and both resulted with successes but in one case we converted it to the transvaginal way. The overall success rate of the transcolonic removal of the proximal colon in all published cases was 12/15 (80%).

Transcolonic extraction of ileocolic resection has been first described for Crohn's disease[2]. Contrary to us, authors divided the mesentery close to the bowel for easier extraction. We believe that some modifications such as intracorporeal mesenteric division can reduce the largest diameter of the specimen and let the transcolonic extraction[6]. As a major morbidity, two postoperative intaabdominal abscesses were reported in the same study[2]. We believe that the main reason of high abdominal infection rate was related with the obstructed terminal ileum. In this study, the authors let the terminal ileum remained open freely to the abdomen for a long operating time. The authors created a side to side ileocolic anastomosis first and later they took out the specimen through this anastomosis. Till the end of the extraction, the distended small bowel went on to contaminate the abdomen. As a difference, we took the specimen into the colon before the anastomosis and the terminal ileum stayed as closed during the extraction time. The terminal ileum was opened just before the anastomosis and the common orifice of the linear stapler was closed immediately. We observed no deep or superficial surgical site infections.

For the first time, we reported that a right-hemicolectomy material was removed through the remnant colon. As mentioned before, Eshuis *et al*[2] preferred only ileocolic specimens, similarly Takayama *et al*[4] reported a case of ileocolic resection for a polyp. Lastly Saad *et al*[3] described a transverse colon resection for a polyp and extracted it through the transcolonic route. Those reported cases with owns all demonstrated that

transcolonic specimen extraction for ileocolic resection, transverse colon resection or even right hemi-colectomy is feasible in selected patients.

As a natural orifice surgery, transcolonic specimen extractions for some right-sided colonic resections and combination with intracorporeal anastomosis let to avoid mini-laparotomy during laparoscopic surgery.

COMMENTS

Background

At laparoscopic colorectal surgery, the use of natural orifices for colonic specimen extraction is a new concept. It can avoid mini-laparotomy and related morbidities.

Research frontiers

Transcolonic extraction of the proximally resected colonic specimens by colonoscopic assistance can be an attractive method for some selected cases. As far as we know, there are only 12 cases reported yet and here, the authors reported three more patients with laparoscopic right-sided colonic resections. All the specimens were intended to remove through the remnant colon by colonoscopy.

Innovations and breakthroughs

Transcolonic specimen extraction for ileocolic resection or even right hemicolectomy is feasible in selected patients.

Applications

Combination with natural orifice surgery and intracorporeal anastomosis avoids mini-laparotomy for specimen extraction or anastomosis.

Terminology

NOTES: Natural orifice transluminal endoscopic surgery. NOSE: Natural orifice specimen extraction.

Peer-review

The authors have performed a good study, the manuscript is interesting.

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P- Reviewer: Ciaccio EJ, Gurkan A
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