Original Article

Clinical impact of laparoscopic intersphincteric resection following neoadjuvant chemoradiotherapy for locally advanced rectal cancer: case-controlled study

Hajime Fujishima[1], Hidefumi Shiroshita[1], Takao Hara[1], Yusuke Itai[1], Noriko Sagawa[1], Jianwei Ma[1], Kentaro Nakajima[1], Yohei Kono[1], Takahiro Hiratsuka[1], Kosuke Suzuki[1], Tomonori Akagi[1], Tomotaka Shibata[1], Yoshitake Ueda[2], Manabu Tojigamori[1], Tsuyoshi Etoh[1], Norio Shiraishi[2], Masafumi Inomata[1]

[1]Department of Gastroenterological and Pediatric Surgery, [2]Comprehensive Surgery for Community Medicine, Oita University Faculty of Medicine, Oita, Japan

Contributions: (I) Conception and design: H Fujishima, H Shiroshita, M Inomata; (II) Administrative support: M Inomata, N Shiraishi; (III) Provision of study materials or patients: All authors; (IV) Collection and assembly of data: H Fujishima, H Shiroshita; (V) Data analysis and interpretation: H Fujishima, H Shiroshita; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Hidefumi Shiroshita, MD, PhD. Department of Gastroenterological and Pediatric Surgery, Oita University Faculty of Medicine, Hasama-machi, Oita 879-5593, Japan. Email: hshiro@oita-u.ac.jp.

Background: Recently, laparoscopic (Lap) intersphincteric resection (ISR) for low-lying rectal cancer is gradually permeating worldwide. However, the usefulness of Lap-ISR after neoadjuvant chemoradiotherapy (NCRT) has not been clarified. This retrospective study aimed to evaluate the feasibility of Lap-ISR after NCRT for locally advanced low-lying rectal cancer.

Methods: Fourteen patients with primary locally low-lying rectal cancer were enrolled in this study and underwent curative Lap-ISR between January 2008 and December 2011. Seven patients underwent Lap-ISR after NCRT (NCRT group) and seven patients underwent Lap-ISR without NCRT (non-NCRT group). Patient characteristics, short-term outcomes, postoperative anal function, and long-term oncological outcomes were evaluated and compared between the groups.

Results: The tumor diameter was significantly larger in the NCRT group than the non-NCRT group (38±7 and 28±9 mm, respectively; P=0.04) and cStage was significantly more advanced in the NCRT group than the non-NCRT group (P=0.02). There were no significant differences in operative data or postoperative course between the groups. The Wexner score measured 5 years after initial surgery was significantly higher the NCRT group than the non-NCRT group (8.8±4.1 and 4.6±1.9, respectively; P=0.04). There were no significant differences in local recurrence rate, distant recurrence rate, or cancer-specific death rate between the two groups (median follow-up period was 60 months).

Conclusions: Lap-ISR after NCRT is a feasible treatment option based on short-term outcomes, long-term oncological outcomes, and postoperative anal function. These data suggest that Lap-ISR after NCRT may be an appropriate treatment option for locally advanced low-lying rectal cancer.

Keywords: Laparoscopic intersphincteric resection (Lap-ISR); neoadjuvant chemoradiotherapy; rectal cancer

Received: 09 March 2018; Accepted: 25 March 2018; Published: 23 April 2018.

doi: 10.21037/ales.2018.03.14

View this article at: http://dx.doi.org/10.21037/ales.2018.03.14

Introduction

In Western countries, neoadjuvant chemoradiotherapy (NCRT) is a standard treatment option for locally advanced rectal cancer. In addition, total mesorectal excision (TME) has been shown to reduce the local recurrence rate (1-3). In Japan, TME or tumor-specific mesorectal excision followed by adjuvant chemotherapy without preoperative treatment is a standard strategy in locally advanced rectal cancer patients, and lateral lymph node dissection is also performed in patients with locally advanced low-lying rectal cancer (4,5). The benefits of NCRT in locally advanced rectal cancer patients include decreased local recurrence and preservation of the anal sphincter (6-8); however, a prognostic impact was not clarified. Therefore, we conducted a multicenter phase II study to evaluate the safety and efficacy of NCRT in patients with locally advanced rectal cancer (9).

Intersphincteric resection (ISR) for low-lying rectal cancer is an attractive procedure for preserving anal function. Previously, abdominoperineal resection (APR) was the only surgical treatment option for low-lying rectal cancer; however, this method lowers quality of life (QOL). ISR can be performed to avoid permanent colostomy in patients whose tumor does not involve the external sphincter.

Recently, laparoscopic (Lap) surgery for colorectal cancer has become widespread because it is minimally invasive and allows for expansion of the visual field during surgery, which can lead to better preservation of the autonomic nerves (10-12). Although several studies have suggested that Lap surgery can be performed safely in colorectal cancer patients (13,14), the usefulness of Lap-ISR after NCRT has not been clarified.

The aim of this study was to evaluate the feasibility of Lap-ISR after NCRT for locally advanced low-lying rectal cancer in terms of short-term outcomes, anal function, and prognosis.

Methods

Patients

Fourteen patients with primary low-lying rectal cancer were enrolled in this study and underwent curative Lap-ISR in our department between January 2008 and December 2011. Seven patients underwent Lap-ISR after NCRT (NCRT group) and seven patients underwent Lap-ISR without NCRT (non-NCRT group).

NCRT

The indication for NCRT in patients with rectal cancer is as follows: (I) histologically proven rectal adenocarcinoma; (II) tumor located in the lower rectum (Rb, P) defined by the Japanese Classification of Colorectal Carcinoma (8th edition) (15); (III) cancer classified as T3-4 and M0 according to the TNM classification system; (IV) no bowel obstruction; (V) sufficient organ function; and (VI) no history of chemotherapy or radiotherapy. This study was approved by the Ethical Committee of our institution, and this study was registered in ResearchRegistry.com as researchregistry3293. All patients included in this study provided written informed consent because NCRT for rectal cancer is not a standard treatment option in Japan. The chemoradiotherapy (CRT) regimen consisted of two cycles of chemotherapy with S-1 (80 mg/m^2 on days 1–5, 8–12, 22–26, and 29–33) and irradiation (total 45 Gy/25 fr, 1.8 Gy/day on days 1–5, 8–12, 15–19, 22–26, and 29–33). The irradiation range was determined as precisely as possible using 3D-CT. Surgery was performed within 6–8 weeks after NCRT treatment.

Surgery

Lap-ISR is adopted as the principle procedure in our institution for low-lying rectal cancer with the following criteria: (I) inferior edge of the tumor is >2 cm from the dentate line; (II) well-differentiated type of adenocarcinoma; (III) T1–2N0M0 cancer; (IV) conserved anal function; (V) the patient wishes to preserve anal function; and (VI) good response to NCRT. The latter was added to the indication in 2009. A good response at our institution is characterized by (I) tumor reduction from cT3–4 to cT2 or less and (II) negative lymph node metastasis.

Lap-ISR is performed by qualified surgeons of endoscopic surgical skill qualification system (ESSQS) of the Japanese Society of Endoscopic Surgery (JSES) (16,17). Lap-ISR was performed using the following methods (18-20): first, the left side of the colon was mobilized by mediolateral retroperitoneal dissection. Second, lymph node dissection around the inferior mesenteric artery and ligation of the artery at the level of origin or preservation of the left colonic artery were performed. The first and second procedures were performed in the reverse order with autonomic nerve preservation. Third, mobilization of the rectum and TME were performed as close as possible to the pelvic floor to make the transanal approach easier. The

surgical anal canal, defined as the anorectal angle to the anal verge, was circumferentially divided from the puborectal muscle and external sphincter. These first three procedures were performed laparoscopically. Fourth, the transanal procedure was then performed. Distal mucosa that was more than 1 cm away from the tumor was incised, and a partial intersphincteric incision was made circumferentially. The laparoscopically and transanally dissected planes were connected, and the specimen was pulled out through the anus. A coloanal anastomosis was performed using transanal hand-sewn suturing, with most patients undergoing side-to-end coloanal anastomosis. Finally, a diverting ileostomy was performed.

Evaluation

Patient characteristics were evaluated in terms of age, gender, body mass index (BMI), mean tumor diameter, distance from the tumor edge to the dentate line, clinical and pathological TNM factors, and residual tumor. Short-term outcomes, including operation time, estimated intraoperative blood loss, intraoperative blood transfusion, intra- and postoperative complications (grade III/IV according to the Clavien-Dindo Classification), and postoperative hospitalization were evaluated and compared between the groups. Anal functional assessment was performed 2 and 5 years after Lap-ISR with respect to stool frequency, fecal urgency, difficult evacuation, fecal incontinence, daytime soiling, nighttime soiling, gas incontinence, pad usage, lifestyle alterations, and Wexner score. Prognosis was evaluated by the incidence of local recurrence, distant metastasis, and cancer-specific death.

Statistical analysis

Quantitative data are provided as a median and range. The differences between the two groups were assessed by the Chi-squared test, Fisher's exact test, Student-t test, or Mann-Whitney U test as appropriate. These analyses were conducted using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan version 1.33) (21), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria version 3.3.1). More precisely, it is a modified version of R commander (version 2.3.0) designed to add statistical functions frequently used in biostatistics. A P-value of less than 0.05 was considered statistically significant.

Results

Patient characteristics

Patient characteristics are presented in *Table 1*. No significant differences were observed in age, gender, BMI, distance from the tumor edge to the dentate line, pT, pN, pStage, and residual tumor. The tumor diameter was significantly larger in the NCRT group than in the non-NCRT group (38±7 and 28±9 mm, respectively; P=0.04). cT was significantly deeper (P=0.02) and cStage was significantly more advanced (P=0.02) in the NCRT group. The incidence of cN-positivity was significantly higher in the NCRT group than in the non-NCRT group (5/7 and 0/7, respectively; P=0.02).

Short-term outcomes

Short-term outcomes are summarized in *Table 2*. The median time of surgery were 452 and 410 min in the NCRT and non-NCRT groups (P=0.13), respectively, and the estimated intraoperative blood loss (median) was 190 and 120 mL, respectively (P=0.25). Intraoperative blood transfusion was not performed in either group and no intraoperative complications were observed. Postoperative complications occurred in three patients. One patient in the NCRT group had anastomotic stenosis. In the non-NCRT group, one patient had pelvic abscess and one had bleeding and pelvic abscess (P=1.00). Postoperative hospitalization time (median) was not significantly different between the NCRT and non-NCRT groups (24 and 26 days, respectively; P=0.61). The stoma was not closed in two patients in the NCRT group; one patient had paraaortic lymph node recurrence and the other had metachronous gastric cancer. Ileostomy was re-established in one patient from the NCRT group because of local recurrence.

Anal function

The postoperative anal function 2 and 5 years after the initial surgery are presented in *Table 3* and *Table 4*, respectively. Two patients in the NCRT group were excluded from *Table 3* because of open ileostomy, one had paraaortic lymph node recurrence and the other had metachronous advanced gastric cancer. One patient in the NCRT group with local recurrence was also excluded due to re-established ileostomy 3 years after the initial surgery. There were no significant differences in anal function

Table 1 Clinicopathological characteristics

Variables	NCRT group (n=7)	Non-NCRT group (n=7)	P
Age (years); median [range]	61 [47–73]	59 [40–79]	0.70
Gender			1.00
Male	5	4	
Female	2	3	
BMI (kg/m^2); median (range)	22.3 (19.5–27.2)	20.5 (18.4–29.4)	0.56
Tumor diameter (mm); mean ± SD	38±7	28±9	0.04
Distance from DL (mm); median [range]	20 [20–25]	20 [20–30]	1.00
cT			0.02
1/2	0	5	
3	7	2	
cN			0.02
Negative	2	7	
Positive	5	0	
cStage			0.02
I	0	5	
II/III	7	2	
pT (ypT)			0.51
0 (CR)	2	0	
1/2	2	4	
3	3	3	
pN (ypN)			0.56
Negative	4	6	
Positive	3	1	
pStage (ypStage)			0.14
0 (CR)	2	0	
I	1	4	
II/III	4	3	
Residual tumor			1.00
R0	6	7	
R1	1	0	

NCRT, neoadjuvant chemoradiotherapy.

between groups 2 years after initial surgery (*Table 3*). Five years after initial surgery, the Wexner score (*Table 4*) was significantly higher in the NCRT group than the non-NCRT group (8.8±4.1 and 4.6±1.9, respectively; P=0.04).

Long-term oncological outcomes

Long-term oncological outcomes are summarized in *Table 5*. The median follow-up period for both groups was 60 months. No significant differences were observed in the

Table 2 Short-term outcomes

Variables	NCRT group (n=7)	Non-NCRT group (n=7)	P
Operation time (min); median [range]	452 [356–685]	410 [250–489]	0.13
Blood loss (mL); median [range]	190 [100–460]	120 [20–360]	0.25
Intraoperative blood transfusion	0	0	-
Intraoperative complications[a]			-
Absent	7	7	
Present	0	0	
Postoperative complications[a]			1.00
Absent	6	5	
Present	1	2[b]	
Anastomotic stenosis	1	0	
Bleeding	0	1	
Pelvic abscess	0	2	
Hospitalization (days); median [range]	24 [21–36]	26 [14–92]	0.61
Ileostomy			
Not closed (diverting stoma)	2	-	
Recurrence	1	-	
Metachronous gastric cancer	1	-	
Re-established (local recurrence)	1	-	

[a], Grade III/IV according to the Clavien-Dindo Classification; [b], There is some overlapping. NCRT, neoadjuvant chemoradiotherapy.

Table 3 Postoperative anal functions (p/o 2 years)

Variables	NCRT group (n=5)	Non-NCRT group (n=7)	P
Stool frequency; mean ± SD	3.8±3.1	2.7±1.6	0.44
Fecal urgency	3 (60%)	3 (43%)	1.00
Difficult evacuation	3 (60%)	3 (43%)	1.00
Fecal incontinence	2 (40%)	2 (29%)	1.00
Day time soiling	2 (40%)	1 (14%)	0.52
Night time soiling	2 (40%)	1 (14%)	0.52
Incontinence to gas	3 (60%)	3 (43%)	1.00
Pad usage	2 (40%)	0 (0%)	0.15
Lifestyle alteration	4 (80%)	4 (57%)	0.86
Wexner's score; mean ± SD	10.0±5.0	5.9±2.0	0.07

Two cases in the NCRT group were excluded because of open ileostoma due to paraaortic lymph node recurrence and metachronous gastric cancer. NCRT, neoadjuvant chemoradiotherapy.

Table 4 Postoperative anal functions (p/o 5 years)

Variables	NCRT group (n=4)	Non-NCRT group (n=7)	P
Stool frequency; mean ± SD	4.3±2.4	2.3±1.4	0.11
Fecal urgency	2 (50%)	1 (14%)	0.49
Difficult evacuation	2 (50%)	2 (40%)	0.58
Fecal incontinence	1 (25%)	0 (0%)	0.36
Daytime soiling	1 (25%)	0 (0%)	0.36
Nighttime soiling	1 (25%)	0 (0%)	0.36
Incontinence to gas	2 (50%)	1 (14%)	0.49
Pad usage	2 (50%)	0 (0%)	0.11
Lifestyle alteration	4 (100%)	6 (86%)	1.00
Wexner score; mean ± SD	8.8±4.1	4.6±1.9	0.04

One case in the NCRT group was excluded because of re-established ileostoma due to local recurrence. NCRT, neoadjuvant chemoradiotherapy.

Table 5 Long-term outcomes

Variables	NCRT group (n=7)	Non-NCRT group (n=7)	P
Recurrence	4 (57%)	0 (0%)	0.07
Local	1 (14%)	0 (0%)	1.00
Distant	4 (57%)	0 (0%)	0.07
Cancer-specific death	2 (29%)	0 (0%)	0.46

One patient in the NCRT group had both local and distant recurrence. NCRT, neoadjuvant chemoradiotherapy.

incidence of overall recurrence or cancer-specific death. In the NCRT group, local recurrence was observed in one patient who also suffered from liver metastases and died 59 months after the initial surgery. Distant recurrences were observed in four patients in the NCRT group. One had liver metastasis and local recurrence. Two patients had lung recurrence and one had paraaortic lymph node recurrence. Cancer-specific deaths were observed in two patients in NCRT group; one with local recurrence and liver metastasis, and one had paraaortic lymph node recurrence after 4 months, who died 20 months after initial surgery.

Discussion

The present data showed that the clinical stage of patients in the NCRT group was significantly more advanced than that of those in the non-NCRT group. Nevertheless, the incidence of local recurrence was not significantly increased, and severe anal dysfunction was not observed in the NCRT group. Lap-ISR after NCRT contributed in control of local recurrence and maintaining QOL in the postoperative course of patients with locally advanced low-lying rectal cancer. The present data suggest that Lap-ISR after NCRT can be a therapeutic strategy for some patients who may benefit from NCRT.

Lap-ISR was adopted in our department as the principal procedure for low-lying rectal cancer. In cases of locally advanced low-lying rectal cancer, deeper than T3, with possible lateral lymph node metastases, NCRT was performed with the aim of local control. Patient with a good response to NCRT and advanced patients with a desire to preserve anal function were added Lap-ISR indication under informed consent. The Lap-ISR procedure was described in previous reports (18-20). We attempted to preserve the autonomic nerve and laparoscopically treat around the anal canal as far as possible.

There were initial concerns that NCRT may lead to changes in operation fields into edematous and adhesive;

however, studies have demonstrated that no significant differences are observed in operation data and incidences of intra- and postoperative complications between surgery alone and after NCRT in patients with rectal cancer (22,23). In addition, the safety of Lap surgery after NCRT for lower rectal cancer was demonstrated in a previous report (24). In our present study, patients in the NCRT group had longer operative time and larger intraoperative blood loss than those in the non-NCRT group. However, the differences in operative findings and complications between patients in the two groups were not significant.

It is a general concern that NCRT for rectal cancer may cause anal dysfunction (25,26). A comparison of the Wexner score between the NCRT and non-NCRT groups showed no significant differences in postoperative anal function 2 years after the initial surgery but were observed 5 years after the initial surgery. Anal dysfunction in the NCRT group was considered difficult to improve. However, there were no cases in which the physician had to perform surgery due to anal dysfunction. In our opinion, setting a strict irradiation range during 3D CT and visual magnification of the laparoscope might contribute to the preservation of anal function.

Previous reports suggest a benefit of neoadjuvant radiotherapy (NRT) that reduces local recurrence rate and prolongs overall survival (OS) and cancer-specific survival for long-term oncological outcomes in rectal cancer (27-29). NRT and NCRT for rectal cancer were compared with EORT trial 22921, FFCD9203, and Polish trial 9203 (30-32). According to these data, OS was not significantly different in the NRT and NCRT groups. Although, the NCRT group included more advanced cases than the non-NCRT group, the local recurrence rate in the NCRT group was not inferior to the non-NCRT group in our study. Considering patients who underwent Lap-APR after NCRT in our department during the same time period, the local recurrence rate of Lap-ISR after NCRT was similar to that of Lap-APR after NCRT [1/7 (14.3%) and 0/5 (0%), respectively; P=1.00]. Accordingly, one of the aims of NCRT, such as control of local recurrence, was accomplished.

ISR after NCRT was reported to be feasible in patients with stage I/II lower rectal cancer (33); however, our present study included patients with stage III lower rectal cancer. Some studies have suggested that patients with a pathologic complete response (pCR) show satisfactory long-term prognosis (34,35). Our study included two patients with pCR who achieved more than 5 years of survival without recurrence. In addition, Rullier *et al.* reported that no significant differences were observed in short- and long-term outcomes between local excision and TME in the patients with a good response after NCRT for low-lying rectal cancer (36). Accordingly, we considered that predicting the effect of NCRT in rectal cancer patients is very important.

Limitations of the present study include the small sample size and the retrospective design. The present retrospective data were likely influenced by selection biases because the NCRT group included more advanced cases than the non-NCRT group. Hence, the present observations require confirmation in prospective studies assessing short- and long-term outcomes of Lap-ISR after NCRT. The results of an ongoing phase II trial of NCRT for rectal cancer (9) are expected. Additionally, more long-term observation is necessary because of possible late adverse effects of NRT treatment.

In conclusion, Lap-ISR after NCRT is feasible in terms of short-term outcomes, anal function, and prognosis. These data suggest that Lap-ISR after NCRT may be an appropriate treatment option for locally advanced low-lying rectal cancer patients.

Acknowledgments

Funding: None.

Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/ales.2018.03.14). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethical Committee of our institution, and this study was registered in ResearchRegistry.com as researchregistry3293. All patients included in this study provided written informed consent.

References

1. MacFarlane JK, Ryall RD, Heald RJ. Mesorectal excision for rectal cancer. Lancet 1993;341:457-60.
2. Enker WE, Thaler HT, Cranor ML, et al. Total mesorectal excision in the operative treatment of carcinoma of the rectum. J Am Coll Surg 1995;181:335-46.
3. Aitken RJ. Mesorectal excision for rectal cancer. Br J Surg 1996;83:214-6.
4. Sugihara K, Kobayashi H, Kato T, et al. Indication and benefit of pelvic sidewall dissection for rectal cancer. Dis Colon Rectum 2006;49:1663-72.
5. Watanabe T, Itabashi M, Shimada Y, et al. Japanese Society for Cancer of the Colon and Rectum (JSCCR) Guidelines 2014 for treatment of colorectal cancer. Int J Clin Oncol 2015;20:207-39.
6. Chang PK, Chiang MH, Jao SW, et al. The outcome of 5-fluorouracil chemotherapy after the completion of neoadjuvant chemoradiotherapy, administered until 2 weeks before rectal cancer resection. J Chin Med Assoc 2015;78:475-80.
7. Sauer R, Becker H, Hohenberger W, et al. Preoperative versus postoperative chemoradiotherapy for rectal cancer. N Engl J Med 2004;351:1731-40.
8. Hyams DM, Mamounas EP, Petrelli N, et al. A clinical trial to evaluate the worth of preoperative multimodality therapy in patients with operable carcinoma of the rectum: a progress report of National Surgical Breast and Bowel Project Protocol R-03. Dis Colon Rectum 1997;40:131-9.
9. Inomata M, Akagi T, Nakajima K, et al. Prospective feasibility study to evaluate neoadjuvant-synchronous S-1 + RT for locally advanced rectal cancer: a multicenter phase II trial (UMIN ID: 03396). Jpn J Clin Oncol 2013;43:321-3.
10. Kitano S, Inomata M, Mizusawa J, et al. Survival outcomes following laparoscopic versus open D3 dissection for stage II or III colon cancer (JCOG0404): a phase 3, randomised controlled trial. Lancet Gastroenterol Hepatol 2017;2:261-8.
11. Kuroyanagi H, Inomata M, Saida Y, et al. Gastroenterological surgery: large intestine. Asian J Endosc Surg 2015;8:246-62.
12. Toda S, Kuroyanagi H. Laparoscopic surgery for rectal cancer: current status and future perspective. Asian J Endosc Surg 2014;7:2-10.
13. Yamamoto S, Inomata M, Katayama H, et al. Short-term surgical outcomes from a randomized controlled trial to evaluate laparoscopic and open D3 dissection for stage II/III colon cancer: Japan Clinical Oncology Group Study JCOG 0404. Ann Surg 2014;260:23-30.
14. Bonjer HJ, Deijen CL, Abis GA, et al. A randomized trial of laparoscopic versus open surgery for rectal cancer. N Engl J Med 2015;372:1324-32.
15. Rectum JSfCoCa. Japanese Classification of Colorectal Carcinona (8th edition). Kanahara Publications, Tokyo in Japanese 2013.
16. Sakai Y, Kitano S. Practice Guidelines on Endoscopic Surgery for qualified surgeons by the Endoscopic Surgical Skill Qualification System. Asian J Endosc Surg 2015;8:103-13.
17. Tanigawa N, Lee SW, Kimura T, et al. The Endoscopic Surgical Skill Qualification System for gastric surgery in Japan. Asian J Endosc Surg 2011;4:112-5.
18. Fujii S, Yamamoto S, Ito M, et al. Short-term outcomes of laparoscopic intersphincteric resection from a phase II trial to evaluate laparoscopic surgery for stage 0/I rectal cancer: Japan Society of Laparoscopic Colorectal Surgery Lap RC. Surg Endosc 2012;26:3067-76.
19. Saito N, Ito M, Kobayashi A, et al. Long-term outcomes after intersphincteric resection for low-lying rectal cancer. Ann Surg Oncol 2014;21:3608-15.
20. Saito N, Sugito M, Ito M, et al. Oncologic outcome of intersphincteric resection for very low rectal cancer. World J Surg 2009;33:1750-6.
21. Kanda Y. Investigation of the freely available easy-to-use software 'EZR' for medical statistics. Bone Marrow Transplant 2013;48:452-8.
22. Denost Q, Laurent C, Paumet T, et al. Laparoscopic surgery for rectal cancer: preoperative radiochemotherapy versus surgery alone. Surg Endosc 2012;26:1878-83.
23. Valenti V, Hernandez-Lizoain JL, Baixauli J, et al. Analysis of early postoperative morbidity among patients with rectal cancer treated with and without neoadjuvant chemoradiotherapy. Ann Surg Oncol 2007;14:1744-51.
24. Kusano T, Inomata M, Hiratsuka T, et al. A comparison of laparoscopic and open surgery following pre-operative chemoradiation therapy for locally advanced lower rectal cancer. Jpn J Clin Oncol 2014;44:305-10.

25. Ozgen Z, Ozden S, Atasoy BM, et al. Long-term effects of neoadjuvant chemoradiotherapy followed by sphincter-preserving resection on anal sphincter function in relation to quality of life among locally advanced rectal cancer patients: a cross-sectional analysis. Radiat Oncol 2015;10:168.
26. Canda AE, Terzi C, Gorken IB, et al. Effects of preoperative chemoradiotherapy on anal sphincter functions and quality of life in rectal cancer patients. Int J Colorectal Dis 2010;25:197-204.
27. Folkesson J, Birgisson H, Pahlman L, et al. Swedish Rectal Cancer Trial: long lasting benefits from radiotherapy on survival and local recurrence rate. J Clin Oncol 2005;23:5644-50.
28. Swedish Rectal Cancer Trial CB, Dahlberg M, Glimelius B, Påhlman L, Rutqvist LE, Wilking N. Improved survival with preoperative radiotherapy in resectable rectal cancer. Swedish Rectal Cancer Trial. N Engl J Med 1997;336:980-7.
29. Camma C, Giunta M, Fiorica F, et al. Preoperative radiotherapy for resectable rectal cancer: A meta-analysis. Jama 2000;284:1008-15.
30. Bosset JF, Collette L, Calais G, et al. Chemotherapy with preoperative radiotherapy in rectal cancer. N Engl J Med 2006;355:1114-23.
31. Gerard JP, Conroy T, Bonnetain F, et al. Preoperative radiotherapy with or without concurrent fluorouracil and leucovorin in T3-4 rectal cancers: results of FFCD 9203. J Clin Oncol 2006;24:4620-5.
32. Bujko K, Nowacki MP, Nasierowska-Guttmejer A, et al. Long-term results of a randomized trial comparing preoperative short-course radiotherapy with preoperative conventionally fractionated chemoradiation for rectal cancer. Br J Surg 2006;93:1215-23.
33. Lee SY, Jo JS, Kim HJ, et al. Prognostic factors for low rectal cancer patients undergoing intersphincteric resection after neoadjuvant chemoradiation. J Surg Oncol 2015;111:1054-8.
34. Janjan NA, Crane C, Feig BW, et al. Improved overall survival among responders to preoperative chemoradiation for locally advanced rectal cancer. Am J Clin Oncol 2001;24:107-12.
35. Capirci C, Valentini V, Cionini L, et al. Prognostic value of pathologic complete response after neoadjuvant therapy in locally advanced rectal cancer: long-term analysis of 566 ypCR patients. Int J Radiat Oncol Biol Phys 2008;72:99-107.
36. Rullier E, Rouanet P, Tuech JJ, et al. Organ preservation for rectal cancer (GRECCAR 2): a prospective, randomised, open-label, multicentre, phase 3 trial. Lancet 2017;390:469-79.

doi: 10.21037/ales.2018.03.14
Cite this article as: Fujishima H, Shiroshita H, Hara T, Itai Y, Sagawa N, Ma J, Nakajima K, Kono Y, Hiratsuka T, Suzuki K, Akagi T, Shibata T, Ueda Y, Tojigamori M, Etoh T, Shiraishi N, Inomata M. Clinical impact of laparoscopic intersphincteric resection following neoadjuvant chemoradiotherapy for locally advanced rectal cancer: case-controlled study. Ann Laparosc Endosc Surg 2018;3:37.

