Defecation disorder and anal function after surgery for lower rectal cancer in elderly patients

Takahiro Korai | Emi Akizuki | Kenji Okita | Toshihiko Nishidate | Koichi Okuya | Yu Sato | Atsushi Hamabe | Masayuki Ishii | Takayuki Nobuoka | Ichiro Takemasa

Department of Surgery, Surgical Oncology and Science, Sapporo Medical University, Sapporo, Japan

Correspondence
Ichiro Takemasa, Department of Surgery, Surgical Oncology and Science, Sapporo Medical University, 1 South, 17 West, Chuo-ku, 060-8556, Sapporo, Japan. Email: itakemasa@sapmed.ac.jp

Abstract
Aim: This study aims to investigate the association of patient age with defecation disorders and anal function after lower rectal cancer surgery.

Methods: We retrospectively reviewed the data of 141 consecutive patients with lower rectal cancer who underwent sphincter-preserving operation. The patients were classified into five categories by age thresholds at 65, 70, 75, 80, and 85 years, for disaggregate analysis. Anal manometry was used for measuring the maximum resting pressure, high-pressure zone, and maximum squeeze pressure. Anal manometry was performed preoperatively and at 3, 6, 9, and 12 months postoperatively. The Wexner and low anterior resection syndrome scores were assessed at 1, 3, 6, 9, and 12 months after rectal surgery or stoma closure for patients with ileostomy.

Results: The data of 117 patients were reviewed. No significant differences were found between the younger and elderly groups in any characteristics across the six age groups. The preoperative intra-anal pressures of the elderly patients were slightly lower than those of the younger patients; however, there was no significant difference in the course of postoperative intra-anal pressures. Defecation disorder, as measured by the Wexner and low anterior resection syndrome scores, improved significantly in elderly patients compared to younger patients.

Conclusion: There was no significant difference in the course of postoperative intra-anal pressures between the elderly and younger patients. However, defecation disorders in elderly patients significantly improved compared with younger patients. Sphincter-preserving operation can be a viable treatment option for active elderly patients.

Keywords
elderly, intra-anal pressures, low anterior resection syndrome, rectal cancer, sphincter-preserving operation
1 | INTRODUCTION

Colorectal cancer is the most common cancer in Japan, and approximately 44,000 cases of cancer of the rectosigmoid and rectum are diagnosed annually.1 In 2015, the national cancer center report in Japan showed that rectal cancer generally appears around the age of 40 years, and the number of patients with this type of cancer increases with advancing age.1 The surgical procedure for rectal cancer is determined primarily based on the radical nature of the cancer and the safety of the operation, with preservation of quality of life (QoL) being an additional important consideration. Whether to preserve the anus is an important issue that greatly influences QoL, because most patients prefer anal preservation. Thus, sphincter-preserving operation (SPO) for lower rectal cancer, such as low anterior resection (LAR) and intersphincter resection (ISR), are gaining popularity, and the number of patients who have undergone SPO is increasing.2-4 However, approximately 90% of patients experience defecation disorders after SPO.5,6 This is termed LAR syndrome (LARS), and it negatively impacts the postoperative QoL.5-8

Although the intra-anal pressure after SPO decreases from damage to the anal sphincter or levator ani muscles,9 intra-anal pressure in the elderly is generally lower than that in young patients because the strength of the external and internal sphincter muscles decreases with age.10,11 Although there are reports suggesting an association between intra-anal pressure and LARS, there is little clear evidence to support this.12 Due to the perception that the intra-anal pressure is generally low in the elderly, it is commonly believed that elderly patients may develop severe LARS after SPO. However, we had the opposite hypothesis in our daily practice, in other words, a clinical question arises about whether postoperative defecation dysfunction might be milder in elderly patients.

SPO indication is based on tumor location and depth; however, the influence of factors such as age, intra-anal pressure, and postoperative defecation disorders is unclear. To date, there have been few longitudinal studies investigating defecation disorders and anal function after surgery for lower rectal cancer in elderly patients. Furthermore, the advantages and disadvantages of SPO for lower rectal cancer in the elderly are not clear; clarification regarding these factors may have significant impact on the choice of surgical procedure. Therefore, this study aimed to explore the association of patient age with defecation disorders and anal function after surgery for lower rectal cancer.

2 | METHODS

2.1 | Patients

Data of all participants with lower rectal cancer (within 10 cm from the anal verge) who underwent rectal surgery at Sapporo Medical University, Department of Surgery, Surgical Oncology and Science between January 2016 and December 2018 were retrospectively reviewed (Figure 1). The number of patients with lower rectal cancer within the study period was 173. We identified 141 consecutive patients who underwent SPO (LAR or ISR) for lower rectal cancer based on their operative records. Twenty-eight patients underwent abdominoperineal resection oncolgically, and four patients with performance status (PS) Grade 2 underwent Hartmann’s operation. We excluded 11 patients who had not undergone stoma closure due to recurrence or death (n = 10), or due to patient preference (n = 1); therefore, 130 patients were included in total. Of these, some patients had moved (n = 3) or faced difficulty in traveling to the hospital due to work or complications (n = 10). Finally, 117 patients were included in the study. To investigate whether there is an age inflection point for LARS, we performed a disaggregate analysis by stratifying the patients into six groups according to their age: <65 years, 65-69 years, 70-74 years, 75-79 years, 80-84 years, and >85 years. There was no minimum or maximum age for enrollment in this study.

PS was evaluated according to Eastern Cooperative Oncology Group (ECOG) score prior to surgery. The ECOG-PS classifies patients into different grades, which are as follows: Grade 0, asymptomatic (fully active, able to perform all pre-disease activities without restriction); Grade 1, symptomatic but completely ambulatory (restricted in performing physically strenuous activity but ambulatory and able to carry out work that is light or sedentary in nature, such as light housework, office work); and Grade 2, symptomatic, in bed for <50% of waking hours (ambulatory and capable of all self-care activities but unable to carry out any work activities; up and about in >50% of waking hours).13

This retrospective study was approved by the ethics committee of Sapporo Medical University (IRB number 312-130). The requirement for informed consent was waived due to the retrospective nature of this study, and we used an opt-out approach (https://sapmed surg1.jp/gairai/optout/).

2.2 | Anal manometry

Analysis of anal manometry was performed using three measures. The maximum resting pressure (MRP), measured in mm Hg, is considered the main indicator of internal sphincter muscle pressure. The length of the high-pressure zone (HPZ), measured in millimeters, is interpreted as the internal sphincter muscle length. The maximum squeeze pressure (MSP), measured in mm Hg, is interpreted as the main indicator of external sphincter muscle pressure.14 There is currently little data on the reference value of intra-anal pressures.15 Based on the data from our department, the standard values for intra-anal pressures were as follows (mean ± SD): MRP, 54.8 ± 20.7 (mm Hg); HPZ, 41.0 ± 8.0 (mm); MSP, 187.9 ± 84.0 (mm Hg). Anal manometry was performed to record all three measures preoperatively and at 3, 6, 9, and 12 months postoperatively using an 8-channel anal manometry system (gmms4000 system; Star Medical) on an outpatient basis to investigate the relationship between age and postoperative defecation disorders.
We used the Wexner score to evaluate fecal incontinence, which is the most frequently used tool in previous LARS reports. Five frequency levels (never, rarely, sometimes, usually, and always) were used to assess solid incontinence, liquid incontinence, gas incontinence, pad wearing, and lifestyle alteration. A total score of zero indicated no incontinence and 20 indicated most severe incontinence. Patients completed these questionnaires at 1, 3, 6, 9, and 12 months after rectal surgery and those with ileostomy completed these after stoma closure.

FIGURE 1 Study flowchart. Among 141 consecutive patients who underwent SPO for lower rectal cancer, 117 are included in this study. The patients were classified into six groups according to the following age thresholds: <65, 65-69, 70-74, 75-79, 80-84, and >85 years. SPO, sphincter-preserving operation

2.3 | Questionnaire

We used the Wexner score to evaluate fecal incontinence, which is the most frequently used tool in previous LARS reports. Five frequency levels (never, rarely, sometimes, usually, and always) were used to assess solid incontinence, liquid incontinence, gas incontinence, pad wearing, and lifestyle alteration. A total score of zero indicated no incontinence and 20 indicated most severe incontinence. Patients completed these questionnaires at 1, 3, 6, 9, and 12 months after rectal surgery and those with ileostomy completed these after stoma closure.

The combination of symptoms (i.e. increased bowel frequency, fecal incontinence, evacuatory dysfunction and urge, high frequency of bowel movement, clustering, incomplete evacuation, and diarrhea) that occur after SPO is referred to as LARS. The LARS score measures the severity of postoperative defecation disorders and has been proven to correlate well with QoL. The LARS score was evaluated by a quick, simple, self-administered questionnaire that objectively measured symptoms in patients who undergo SPO. The questionnaire comprised the following five questions: (a) Do you ever have occasions when you cannot control your flatus (wind)?; (b) Do you ever have any accidental leakage of liquid stool?; (c) How often do you open your bowels?; (d) Do you ever have to open your bowels again within 1 hour of the last bowel opening?; and (e) Do you ever have such a strong urge to open your bowels that you have to rush to the toilet? A higher score indicated a worse degree of
LARS; for example, a total score of 42 indicated most severe LARS. We used the Japanese version of the LARS score in this study (https://sapmed-surg1.jp/team/team01b/). Similar to the Wexner score, patients completed these questionnaires at 1, 3, 6, 9, and 12 months after rectal surgery or after stoma closure for patients with ileostomy. All the questionnaires were completed and collected at the outpatient clinic.

2.4 | Statistical analysis

Fisher’s exact test was used to analyze categorical variables, including sex and type of surgery. The student-t test was used to analyze continuous variables, such as body mass index (BMI) and distance to anastomosis from the anal verge. Repeated measures analysis of variance (ANOVA) (Greenhouse-Geisser correction) and a post-hoc Dunnett’s multiple comparison test were used to analyze continuous variables, such as the intra-anal pressures, the Wexner scores, and LARS scores.

All P-values were two sided, and P-values ≤ 0.05 were considered statistically significant. All statistical analyses were performed using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), a graphical user interface for R (The R Foundation for Statistical Computing). More precisely, it is a modified version of the R commander designed to add statistical functions frequently used in biostatistics.

3 | RESULTS

For patients whose follow-up was interrupted due to moving or difficulty in traveling to the hospital after SPO (total n = 13), the questionnaire could not be administered continuously. Therefore, the response rate of the questionnaire was 117/130 (90%) (Figure 1). Table 1 shows the baseline and perioperative characteristics of patients who underwent rectal cancer surgery. No significant differences were found between the six groups in most of the characteristics, including sex (P = .95), BMI (P = .50), ECOG-PS grade (P = .83), tumor location (P = .13), T-stage (P = .54), receipt of neoadjuvant therapy (P = .76), type of surgery (P = .16), and whether transanal total mesorectal excision (P = .06) or lateral lymph node dissection (P = .83) was performed. There were also no significant differences between the distance to anastomosis from the anal verge (P = .25) and the duration until ileostomy closure (P = .89) between the six groups. There were no cases of temporary diverting stoma in the >85 years group, and there was a significant difference between the six groups (P = .02). In the other five groups, a temporary diverting stoma was made in approximately 80%-90% of cases (Table S1).

Trends in preoperative and postoperative intra-anal pressures are shown in Figure 2. There was no significant difference between the six groups with respect to the MRP, HPZ, and MSP (MRP: P = .39, HPZ; P = .82, MSP; P = .34). Preoperative and postoperative intra-anal pressures in all groups are listed in Table S2. Except for MSP in the >85 years group, all other groups showed a significant decrease in intra-anal pressures at 3 months postoperatively compared to the corresponding preoperative values. Subsequently, the intra-anal pressures were found to recover over time (Table S2).

The Wexner and LARS scores were measured at 1, 3, 6, 9, and 12 months after SPO or after stoma closure for patients with

| TABLE 1 Baseline and perioperative characteristics of all eligible patients with lower rectal cancer |
|-----------------------------------------------|
| Characteristics | Eligible patients |
|------------------|-------------------|
| N = 117          |                   |
| Sex              |                   |
| Male             | 69 (59%)          |
| Female           | 48 (41%)          |
| BMI (kg/m²)      | 23.3 ± 3.9        |
| ECOG-PS Grade    |                   |
| 0                | 106 (91%)         |
| 1                | 11 (9%)           |
| Tumor location   |                   |
| Ra               | 44 (37%)          |
| Rb               | 73 (63%)          |
| T-stage          |                   |
| T1               | 15 (13%)          |
| T2               | 23 (20%)          |
| T3               | 73 (62%)          |
| T4               | 6 (5%)            |
| Neoadjuvant therapy |             |
| No               | 62 (53%)          |
| NAC              | 54 (46%)          |
| CRT              | 1 (1%)            |
| Type of surgery  |                   |
| LAR              | 64 (55%)          |
| ISR              | 53 (45%)          |
| Approach         |                   |
| Laparoscopic approach only | 56 (48%) |
| Transanal approach | 61 (52%) |
| LLND             | 25 (20%)          |
| Distance to anastomosis from AV (cm) | 4.0 ± 1.6 |
| Temporary diverting stoma | 96 (82%) |
| The period until stoma closure (months) | 6.7 ± 3.7 |

Note: Data are presented as n (%) unless otherwise stated.

Abbreviations: AV, anal verge; BMI, body mass index; CRT, chemoradiation therapy; ECOG-PS, Eastern Cooperative Oncology Group-Performance status; ISR, intersphincteric resection; LAR, lower anterior resection; LLND, lateral lymph node dissection; NAC, neoadjuvant chemotherapy; TaTME, transanal total mesorectal excision.

a Data are presented as average ± SD.
ileostomy. In particular, the elderly group (75-79 years, 80-84 years, and ≥85 years) had a greater postoperative improvement in the LARS score than the younger group (Figure 3). A post-hoc Dunnett's multiple comparison test revealed that there was a group with significant improvement at already 6 months postoperatively when 1 month postoperatively was used as a control. Both the Wexner and the LARS score showed a significant improvement in most age groups at 12 months postoperatively when using 1 month postoperatively as a control (Figure 4).

**4 | DISCUSSION**

We made two important clinical observations in this study. First, the intra-anal pressures of the elderly patients were slightly lower than those of the younger patients; however, there was no significant difference in the postoperative course of intra-anal pressures. Second, defecation disorder, as measured by the Wexner and LARS scores, improved to a significantly greater extent in elderly patients than in younger patients. Due to the perception that the intra-anal pressure is generally low in the elderly, it is commonly believed that elderly patients may develop severe LARS after SPO. However, we had the opposite hypothesis in our daily practice and the results of this study showed that our hypothesis was correct.

It is generally assumed that intra-anal pressure tends to be lower in elderly patients than in younger patients; this was also observed with respect to preoperative MRP, HPZ, and MSP, which were interpreted as the main indicators of internal or external sphincter muscle pressure in this study. However, no previous study has assessed the relationship between intra-anal pressure and age in patients undergoing lower rectal cancer surgery. SPO, especially ISR, involves the removal of the internal anal sphincter...
muscle, which has a significant impact on postoperative MRP being interpreted as the main indicator of internal sphincter muscle pressure. All intra-anal pressures, including MRP and HPZ preoperatively, which differed between elderly and younger patients, were severely damaged by the SPO and no longer differed according to age. An important finding of this study is that the preoperative intra-anal pressures of the elderly patients were slightly lower than those of the younger patients; however, there was no significant difference in the postoperative course of intra-anal pressures. The fact that the intra-anal pressure decreased in both groups after SPO surgery is considered to have a more significant effect on LARS in the early postoperative period, rather than the increase or decrease of bowel peristalsis. Notably, when the intra-anal pressure recovered over time, the original difference in bowel peristalsis became more noticeable.

Our results show that it is important to actively decide to perform SPO, even in elderly patients, to achieve postoperative patient satisfaction. However, since severe LARS frequently occurs at 3-6 months postoperatively, even in the elderly, due consideration must be made to offer SPO to patients with a good PS (able to go to the bathroom quickly, sometimes 3-4 times an hour and nearly 10 times a day).

This study had three main limitations. First, the sample size was small, especially with respect to the number of elderly patients; consequently, this might have weakened the statistical power of the study. Second, this study was conducted on patients with ECOG PS Grade 0-1 (those who were in good general condition). The results of SPO in patients with ECOG PS Grade 2 or higher were not elucidated. We believe that further prospective studies are needed to accumulate more cases and verify our findings. Third, whether the patients had preoperative fecal incontinence or defecation disorder was not evaluated in this study. We considered that the preoperative Wexner and LARS scores are not necessarily an accurate reflection of the patient’s preoperative defecation function because patients with lower rectal cancer often experience fecal disorder due to the presence of a tumor, and this is not reflective of the patient’s true bowel habits.

In conclusion, there was no significant difference in the postoperative course of intra-anal pressures between the elderly and younger patients; however, defecation disorders in elderly patients significantly improved after surgery compared with younger patients. These findings may help determine the optimal surgical procedure for lower rectal cancer in elderly patients. SPO can be a viable treatment option for active elderly patients.
ACKNOWLEDGEMENTS
We would like to thank Editage (www.editage.jp) for English language editing. We thank Dr Shiro Hinotsu (Department of Biostatistics and Clinical Epidemiology, Sapporo Medical University, Sapporo, Japan) for the statistical support.

DISCLOSURE
Conflict of interest: Authors declare no conflict of interest for this article.
Ethical statements: The protocol for this research project has been approved by a suitably constituted Ethics Committee of Sapporo Medical University and it conforms to the provisions of the Declaration of Helsinki (Committee of Sapporo Medical University, Approval No. 312-130). The requirement for informed consent was waived due to the retrospective nature of this study.

ORCID
Takahiro Korai https://orcid.org/0000-0002-5131-4953
Atsushi Hamabe https://orcid.org/0000-0001-5535-3514
Ichiro Takemasa https://orcid.org/0000-0003-1595-2453
REFERENCES

1. Center for cancer control and information services [internet]. National Cancer Center; 2019. Available from: http://ganjo-ho.jp/reg_stat/statistics/stat/summary.html

2. Shirouzu K, Ogata Y, Araki Y, Sato Y. A new ultimate anus-preserving operation for extremely low rectal cancer and for anal canal cancer. Tech Coloproctol. 2003;7(3):203–6.

3. Shirouzu K, Murakami N, Akagi Y. Intersphincteric resection for very low rectal cancer: a review of the updated literature. Ann Gastroenterol Surg. 2017;1(1):24–32.

4. Molnar C, Nicolescu C, Grigorescu BL, et al. Comparative oncological outcomes and survival following surgery for low rectal cancer – a single center experience. Rom J Morphol Embryol. 2019;60(3):847–52.

5. Akizuki E, Matsuno H, Satoyoshi T, et al. Validation of the Japanese version of the low anterior resection syndrome score. World J Surg. 2018;42(8):2660–7.

6. Emmertsen KJ, Laurberg S. Rectal Cancer Function Study Group. Impact of bowel dysfunction on quality of life after sphincter-preserving resection for rectal cancer. Br J Surg. 2013;100(10):1377–87.

7. Bryant CL, Lunniss PJ, Knowles CH, Thaha MA, Chan CL. Anterior resection syndrome. Lancet Oncol. 2012;13(9):e403–8.

8. Kupsch J, Kuhn M, Matzel KE, et al. To what extent is the low anterior resection syndrome (LARS) associated with quality of life as measured using the EORTC C 30 and CR 38 quality of life questionnaires? Int J Colorectal Dis. 2019;34(3):747–62.

9. Koda K, Yamazaki M, Shuto K, et al. Etiology and management of low anterior resection syndrome based on the normal defecation mechanism. Surg Today. 2019;49(10):803–8.

10. Lundby L, Duelund-Jakobsen J. Management of fecal incontinence after treatment for rectal cancer. Curr Opin Support Palliat Care. 2011;5(1):60–4.

11. Gundling F, Seidl H, Scalercio N, Schmidt T, Schepp W, Pehl C. Influence of gender and age on anorectal function: normal values from anorectal manometry in a large Caucasian population. Digestion. 2010;81(4):207–13.

12. Bjorn MX, Perdawood SK. Manometric assessment of anorectal function after transanal total mesorectal excision. Tech Coloproctol. 2020;24(3):231–6.

13. Oken MM, Creach RH, Tormey DC, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol. 1982;5(6):649–55.

14. Titi MA, Jenkins JT, Urié A, Molloy RG. Correlation between anal manometry and endosonography in females with faecal incontinence. Colorectal Dis. 2008;10(2):131–7.

15. Yoshida K, Nakashima M, Ojima Y, et al. Anal function evaluation test for patients with fecal incontinence. Jpn J Med Technol. 2016;65(4):373–80.

16. Jorge JM, Wexner SD. Etiology and management of fecal incontinence. Dis Colon Rectum. 1993;36(1):77–97.

17. Emmertsen KJ, Laurberg S. Low anterior resection syndrome score: development and validation of a symptom-based scoring system for bowel dysfunction after low anterior resection for rectal cancer. Ann Surg. 2012;255(5):922–8.

18. Juul T, Ahlberg M, Blinding S, et al. Low anterior resection syndrome and quality of life: an international multicenter study. Dis Colon Rectum. 2014;57(5):585–91.

19. Battersby NJ, Boulotis G, Emmertsen KJ, et al. Development and external validation of a nomogram and online tool to predict bowel dysfunction following restorative rectal cancer resection: the POLARS score. Gut. 2018;67(4):688–96.

20. Kanda Y. Investigation of the freely available easy-to-use software “EZR” (easy R) for medical statistics. Bone Marrow Transplant. 2013;48(3):452–8.

21. Kupsch J, Jackisch T, Matzel KE, et al. Outcome of bowel function following anterior resection for rectal cancer-an analysis using the low anterior resection syndrome (LARS) score. Int J Colorectal Dis. 2018;33(6):787–98.

22. Nocera F, Angehrn F, Flue M, et al. Optimising functional outcomes in rectal cancer surgery. Langenbecks Arch Surg. 2020;406:233–50.

23. Koda K, Yamazaki M, Shuto K, et al. Etiology and management of low anterior resection syndrome based on the normal defecation mechanism. Surg Today. 2019;49(10):803–8.

24. Yu SW, Rao SS. Anorectal physiology and pathophysiology in the elderly. Clin Geriatr Med. 2014;30(1):95–106.

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher’s website.

How to cite this article: Korai T, Akizuki E, Okita K, Nishidate T, Okuya K, Sato Y, et al. Defecation disorder and anal function after surgery for lower rectal cancer in elderly patients. Ann Gastroenterol Surg. 2022;6:101–108. https://doi.org/10.1002/ags3.12505