Long-Term Outcomes After Extra-Levator Versus Conventional Abdominoperineal Excision for Low Rectal Cancer

Zhang Haoyu

Capital Medical University

Ganbin Li

Capital Medical University

Ke Cao

Capital Medical University

Zhiwei Zhai

Beijing Chao-Yang Hospital

Guanghui Wei

Beijing Chao-Yang Hospital

Chunxiang Ye

Beijing Chao-Yang Hospital

Baocheng Zhao

Beijing Chao-Yang Hospital

Zhenjun Wang

Beijing Chao-Yang Hospital

Jiagang Han (✉ hjgzhy98@163.com)

Beijing Chao-Yang Hospital

Research Article

Keywords: extralevator abdominoperineal excision, abdominoperineal excision, rectal cancer, survival

Posted Date: November 29th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-1095645/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Purpose

Extralevator (ELAPE) and abdominoperineal excision (APE) are two major surgical approaches for low rectal cancer patients. Although excellent short-term efficacy is achieved in patients undergoing ELAPE, the long-term benefits have not been established. In this study we compared the survival outcomes in low rectal cancer patients who underwent ELAPE and APE.

Methods

One hundred fourteen patients were enrolled, including 68 in the ELAPE group and 46 in the APE group at the Beijing Chaoyang Hospital, Capital Medical University from January 2011 to December 2018. The baseline characteristics, overall survival (OS), progression-free survival (PFS), and local recurrence-free survival (LRFS) were calculated and compared between the two groups.

Results

Demographics and tumor stage were comparable between the two groups. The 5-year PFS (67.2 per cent versus 38.6 per cent, log-rank $P = 0.008$) and LRFS (87.0 per cent versus 62.3 per cent, log-rank $P = 0.047$) were significantly improved in the ELAPE group compared to the APE group, and the survival advantage was especially reflected in patients with pT3 tumors, positive lymph nodes or even those who have not received neoadjuvant chemoradiotherapy. Multivariate analysis showed that APE was an independent risk factor for OS (hazard ratio 3.000, 95 per cent c.i. 1.171 to 4.970, $P = 0.004$) and PFS (hazard ratio 2.730, 95 per cent c.i. 1.506 to 4.984, $P = 0.001$).

Conclusion Compared with APE, ELAPE improved long-term outcomes for low rectal cancer patients, especially among patients with pT3 tumors, positive lymph nodes or those without neoadjuvant chemoradiotherapy.

Introduction

Since introduction, abdominoperineal excision (APE) has been used as a standard surgical procedure for patients with advanced low rectal cancer¹. Due to the complex anatomic structure around and in close proximity to the rectum, the "surgical waist" in the tumor-bearing segment around the sphincter complex may cause a positive circumferential resection margin (CRM) and intraoperative perforation (IOP) when removing the levator muscles². The positive CRM and IOP rates in the APE group have been reported to be as high as 28.2 per cent and 49 per cent, respectively, resulting in an increased risk of local recurrence and distant metastases²⁻⁴.

In 2007, Holm et al.^{5,6} proposed the concept of extralevator abdominoperineal excision (ELAPE), which fully exposes the perineum and pelvic floor easily and resection of the anal canal and levator muscles to avoid a "surgical waist"⁷. Although some studies have concluded that there was no significant difference in positive CRM and IOP rates between ELAPE and APE, the majority of studies have demonstrated superiority of ELAPE^{8,9}. A further study reported that ELAPE reduces the positive CRM and IOP rates to 20.3 per cent and 8.2 per cent, respectively¹⁰.

ELAPE was developed as a response to poor oncologic outcomes with APE; however, many studies with long-term oncologic outcome data have called into question the value of ELAPE^{11–14}. Specifically, a large population-based study from Sweden didn't demonstrate any survival advantage of ELAPE over APE¹². The results from these studies^{11–14}; however, may be limited by short follow-up periods and small sample sizes. Recently, Shen et al.⁶ reported the survival benefit of ELAPE in a long follow-up period compared with APE. Because the superiority of ELAPE when compared to APE is controversial in the recent literature, further studies on this issue are warranted.

Our center began utilizing ELAPE in low rectal cancer patients in 2008¹⁵. In the current study, we compared long-term outcomes between ELAPE and APE procedures, and determined the risk factors that affect long-term survival of patients with low rectal cancer.

Materials And Methods

Patients

This study consisted of patients who underwent ELAPE and APE for low rectal cancer at Beijing Chaoyang Hospital of Capital Medical University between January 2011 and November 2020. During that time period, 1119 patients with advanced rectal cancer underwent surgical resection. Of these patients, 121 consecutive patients with advanced low rectal cancer underwent APE or ELAPE. After exclusions, 114 patients were included in the analysis, including 68 patients who underwent ELAPE and 46 patients who underwent APE (Fig. 1). The inclusion criteria were as follows: 1) rectal malignant tumor determined by histology 2) age: 18 to 80 years; 3) ELAPE or APE; 4) Stage II or III determined by preoperative radiographic tests before neoadjuvant therapy; and 5) American Society of Anesthesiologists (ASA) score I and II. The exclusion criteria were as follows: 1) distant metastases found before surgery; 2) acute intestinal obstruction and 3) recurrent cancer. A treatment plan was formulated for each patient by the multi-disciplinary team. Neoadjuvant chemoradiotherapy was recommended for patients with tumors that were considered to be difficult to achieve R₀ resection. The patients received neoadjuvant chemoradiotherapy as a combination of radiation (2.0 Gy/fraction 5 times per week for 5 weeks) and chemotherapy (CapeOX repeated every 3 weeks or mFoLFoX6 repeated every 2 weeks). Surgery was carried out 8 to 12 weeks following neoadjuvant chemoradiotherapy. Patients were completely random in the selection of surgical approaches. The study was conducted in accordance with the Declaration of

Helsinki and was approved by the local Ethics Committee of Beijing Chaoyang Hospital. All patients provided their informed consent for the use of their data in the study (2011-ke-143).

Surgical procedure

The tumor was indicated for abdominoperineal excision if it invaded the levator or anal sphincter or considered to be low for sphincter salvage by surgeons. ELAPE and APE were carried out by two different groups in this department and the patients were randomly assigned to those groups after admission. The surgeons involved in the study have been appropriately trained in ELAPE or APE and both groups have more than ten years' experience in rectal cancer surgery.

The abdominal portion of ELAPE was performed in the spine position. The procedure mobilized the mesorectum in the plane outside the mesorectal fascia, stopping at the top of the coccyx in the back and below the level of the seminal vesicles or cervix anteriorly to achieve a total mesorectal excision. After a colostomy was formed, the patient was rolled over into the prone position for the perineal approach. The perineum continued to be mobilized along the surface of the levator muscle to the pelvic side wall, meeting the abdominal portion at the start of the levator muscle to entirely remove the levator muscles. The specimens were cylindrical because the levator muscle was still attached to the mesorectum.

APE was performed from the abdominal and perineal portions sequentially in the lithotomy position. The procedure mobilized the mesorectum from the levator muscles. When the rectum was fully mobilized, the surgeon moves in between the legs to perform the perineal portion and the abdominal dissection was performed with excision of the anal canal, including the ischiorectal fat and the lower portions of the levator muscles. There was usually a narrow waist at the lower border of the mesorectum at the level above the levator muscles in the specimen.

Data Collection

The clinicopathologic data, and patient status were all obtained from the database. Measurement of the distance between the lower edge of the tumor and the anus was based on a preoperative MRI. The tumor location was determined by radiographic tests, physical examination, or surgical specimens. Positive CRM was defined as cancer cells detected within 1 mm of the resection margin. The clinical TNM staging before neoadjuvant chemoradiotherapy was determined by preoperative radiographic tests.

Follow-up evaluations were arranged every 3 months for 2 years and every 6 months thereafter. Chest X-ray, abdominal CT, and pelvic MRI were performed annually to detect local recurrences or distant metastases. Follow-up evaluations were performed in the outpatient department and by telephone. This study was ended in April 2021.

The following endpoints were estimated: overall survival (OS), defined as the interval from the date of surgery to the date of death from any cause; progression-free survival (PFS), defined as the interval from the date of surgery to the date of local recurrence or distant metastasis; and local recurrence-free survival

(LRFS), defined as the interval from the date of surgery to the date of local recurrence. Stratified analyses were performed according to postoperative stage, with or without preoperative neoadjuvant chemoradiotherapy.

Statistical Analysis

Statistical analysis was performed based on SPSS 25.0 (IBM Corp., Armonk, NY, USA). Independent t-tests, the Mann-Whitney *U* test, and the chi-square test were used to compare the statistical differences between the two groups. The Kaplan-Meier curve was used to describe the long-term survival trend. Variables that had a statistically significant association (at $P < 0.1$) with survival of patients on univariate analysis were entered into a multivariable model. Results were considered statistically significant at $P < 0.05$.

Results

The median follow-up time was 48.0 months (range 3.0 to 120.0). Of the 114 patients, 14 were lost to follow-up before the endpoint occurred, including 8 [10.5 per cent (8 of 76)] cases in the ELAPE group and 6 [8.8 per cent (6 of 68)] in the APE group; the time from the operation to the most recent follow-up was recorded in the analysis.

Clinical characteristics

There were no significant differences in gender, age, distance from the anal verge, co-morbidities, tumor location, length of postoperative hospitalization, and postoperative complications between the ELAPE and APE groups. Patients who underwent ELAPE were more likely to receive neoadjuvant chemoradiotherapy in this study [45.6 per cent (31 of 68) versus 19.6 per cent (9 of 46), $P=0.004$]. Compared with the APE group, the ELAPE group had a higher proportion of open surgery [30.9 per cent (21 of 68) versus 10.9 per cent (5 of 46), $P=0.012$]. The intraoperative blood loss in the ELAPE group was greater than the APE group (175 versus 100 ml, $P=0.004$). The total operative time in the ELAPE group were significantly longer than the APE group (318 versus 210 min, $P < 0.001$) (Table 1).

Table 1
Comparison of clinical variables of patients between the ELAPE and APE group

	ELAPE (n= 68)	APE (n =46)	P value
Gender [n (%)]			0.829
Male	43 (63.2)	30 (65.2)	
Female	25 (36.8)	16 (34.8)	
Age (yr, x±s)	61.3±11.5	64.8±11.1	0.105
BMI (kg/m ² , x± s)	24.6±3.7	23.8±3.2	0.669
Cardiovascular disease [n (%)]	23 (33.8)	17 (37.0)	0.731
Diabetes mellitus [n (%)]	10 (14.7)	8 (17.4)	0.700
Cerebral disease [n (%)]	3 (4.4)	2 (4.2)	0.949
Distance from anal verge [cm, M (range)]	3.0 (2.0-3.5)	3.0 (2.0-4.0)	0.315
Clinical T stage [n (%)]			0.593
cT ₁₋₂	8(11.8)	7(15.2)	
cT ₃₋₄	60(88.2)	39(84.8)	
Clinical N stage [n (%)]			0.946
cN ₀	38(55.9)	26(44.1)	
cN ₊	30(56.5)	20(43.5)	
Clinical stage [n (%)]			0.717
II	48(70.6)	31(67.4)	
III	20(29.4)	15(32.6)	
Neoadjuvant chemoradiotherapy [n (%)]			0.004*
Yes	31 (45.6)	9 (19.6)	
No	37 (54.4)	37 (80.4)	
Postoperative chemotherapy [n (%)]			0.280
Yes	48 (70.6)	28(60.9)	
No	20 (29.4)	18(39.1)	
Approaches of operation [n (%)]			0.012*
Laparoscopy assisted	47 (69.1)	41 (89.1)	

	ELAPE (n= 68)	APE (n =46)	P value
Open	21 (30.9)	5 (10.9)	
Total operative time [min, M (range)]	318(268-360)	210 (180-275)	<0.001*
Blood loss [ml, M (range)]	175 (100-200)	100 (80-200)	0.004*
Pelvic floor construction [n (%)]			<0.001*
Yes	51 (75.0)	2 (4.3)	
No	17 (25.0)	44 (95.7)	
Combined organ resection [n (%)]			0.802
Yes	2 (2.9)	1 (2.2)	
No	66 (97.1)	45 (97.8)	
Duration of postoperative hospitalization [d, M(range)]	16 (14-21)	16 (12-26)	0.899
Postoperative drainage time [d, M(range)]	12 (9-14)	8 (6-12)	<0.001*
Postoperative complications [n (%)]	19 (27.9)	12 (26.1)	0.827
Abdominal wound healing problem [n (%)]	8 (11.8)	8 (17.4)	0.396
Intestinal obstruction [n (%)]	7 (10.3)	1 (2.2)	0.076
Urinary infection [n (%)]	3 (4.4)	4 (8.7)	0.350
Perineal hernia [n (%)]	3 (4.4%)	1 (2.2%)	0.524

Oncologic characteristics

The tumor characteristics are shown in Table 2. The number of lymph nodes harvested in the ELAPE group was significantly less than the APE group (14 versus 16, $P=0.034$). There was no significant difference between the ELAPE and APE groups in the distance from the lower edge of the tumor to the anus, positive lymph node ratio, clinical T stage, pathologic TN stage, TNM stage, tumor differentiation, lymphovascular invasion, nerve invasion, and positive CRM rates.

Table 2
Comparison of oncologic variables of patients between the ELAPE group and APE group.

	ELAPE (n= 68)	APE (n= 46)	P value
Pathological T stage [n (%)]			0.343
pT ₀₋₂	19(27.9)	15(32.6)	
pT ₃	29(42.6)	23(50.0)	
pT ₄	20(29.4)	8(17.4)	
ypT stage [n (%)]			0.440
ypT ₀₋₂	9(29.0)	3(33.3)	
ypT ₃	12(38.7)	5(55.6)	
ypT ₄	10(32.3)	1(11.1)	
Pathological N stage [n (%)]			0.955
pN ₀	44(64.7)	30(65.2)	
pN ₊	24(35.3)	16(34.8)	
ypN stage [n (%)]			0.687
ypN ₀	22(71.0)	7(77.8)	
ypN ₊	9(29.0)	2(22.2)	
Pathological stage [n (%)]			0.768
I	14(20.6)	12(26.1)	
II	30(44.1)	18(39.1)	
III	24(35.3)	16(34.8)	
Lymph nodes harvested [M (range)]	14(10-17)	16(13-21)	0.034*
Positive positive lymph node ratio [M (range)]	0(0-0.11)	0(0-0.11)	0.941
Histopathology [n (%)]			0.600
Adenocarcinoma	60(88.2)	42(91.3)	
Mucinous/Signet-ring cell	8(11.8)	4(8.7)	
Tumor differentiation [n (%)]			0.306
Well	3(5.0)	0(0)	

	ELAPE (n= 68)	APE (n= 46)	P value
Moderate	53(88.3)	38(90.5)	
Poor	4(6.7)	4(9.5)	
Lymphovascular invasion [n (%)]			0.846
Yes	21(30.9)	15(32.6)	
No	47(69.1)	31(67.4)	
Nerve invasion[n(%)]			0.148
Yes	14(20.6)	15(32.6)	
No	54(79.4)	31(67.4)	
Positive CRM[n (%)]	6(8.8)	8(17.4)	0.172
Incidence of R0 resection	62(91.2)	38(82.6)	0.172

Survival

Compared with the APE group, patients in the ELAPE group had a longer 5-year PFS (67.2 per cent versus 38.6 per cent; log-rank $P=0.008$) and 5-year LRFS (87.0 per cent versus 62.3 per cent; log-rank $P=0.047$). The 5-year OS between the two groups was not statistically different (Fig. 2).

Pathologic T₃ patients in the ELAPE group had a significantly better 5-year OS (82.6 per cent versus 40.1 per cent; log-rank $P=0.021$), 5-year PFS (59.7 per cent versus 28.8 per cent; log-rank $P=0.036$), and 5-year LRFS (90.0 per cent versus 54.3 per cent; log-rank $P=0.007$) than the APE group (Fig. 3). There were no significant differences in OS, PFS, and LRFS between the two groups of patients with pathologic stages T₀₋₂ and T₄ (Fig. 4). Patients with positive lymph nodes in the ELAPE group had a significantly better 5-year PFS (48.7 per cent versus 17.8 per cent; log-rank $P=0.013$) and 5-year LRFS (83.5 per cent versus 33.7 per cent; log-rank $P=0.011$) than the APE group (Fig. 5).

For patients with neoadjuvant chemoradiotherapy, ELAPE group showed better 5-year PFS compared to APE group (64.7 per cent versus 33.3 per cent; log-rank $P=0.031$), but no statistical difference was observed in OS and LRFS between the two groups. Patients without neoadjuvant chemoradiotherapy in the ELAPE group had a significantly better 5-year PFS (68.4 per cent versus 40.7 per cent; log-rank $P=0.047$) than the APE group (Fig. 6).

Univariate and multivariate analyses

Univariate analysis showed the following: operation type, pathologic T stage, positive lymph nodes, positive lymph node ratio, lymphovascular invasion, nerve invasion, and positive CRM were risk factors for OS; operation type, pathologic T stage, positive lymph nodes, positive lymph node ratio, lymphovascular invasion, nerve invasion, and positive CRM were risk factors for PFS; and operation type,

pathologic T stage, positive lymph nodes, tumor differentiation, nerve invasion, and positive CRM were risk factors for LRFS. Multivariate analysis showed the following: APE (hazard ratio 3.000, 95 per cent c.i. 1.171 to 4.970, $P = 0.004$) and advanced pathologic T stage (hazard ratio 2.044, 95 per cent c.i. 1.238 to 3.375, $P = 0.006$) were independent risk factors for OS; APE (hazard ratio 2.730, 95 per cent c.i. 1.506 to 4.984, $P = 0.001$), positive lymph nodes (hazard ratio 1.865, 95 per cent c.i. 0.886 to 3.154, $P = 0.045$), and lymphovascular invasion (hazard ratio 1.882, 95 per cent c.i. 1.057 to 3.354, $P = 0.048$) were independent risk factors for PFS; and positive CRM (hazard ratio 2.648, 95 per cent c.i. 1.084 to 6.866, $P = 0.049$) and advanced pathologic T stage (hazard ratio 1.860, 95 per cent c.i. 1.221 to 4.557, $P = 0.046$) were independent risk factors for LRFS (Supplementary_Tables_1-6).

Discussion

ELAPE has been performed in patients with low rectal cancer in recent years and has resulted in superior oncologic outcomes compared with APE, but controversy exists regarding the long-term survival of this technique^{13,16}. In the current study long-term outcomes of patients undergoing ELAPE and APE were evaluated, and we showed that ELAPE improved survival of patients with low rectal cancer when compared with APE, especially for patients with pT₃ tumors, positive lymph nodes or those without neoadjuvant chemoradiotherapy.

Despite a wider range of resection, the lymph nodes harvested in the ELAPE group were significantly less in number than the APE group. Although more tissue is removed with ELAPE, the number of lymph nodes dissected is not necessarily increased. Alternatively, the effect of a higher proportion of patients receiving neoadjuvant chemoradiotherapy in the ELAPE group. We found that the number of lymph nodes harvested in the patients who received neoadjuvant chemoradiotherapy was significantly less than patients who did not in the ELAPE group (11 versus 15, $P < 0.001$). A nationwide study showed that fewer nodes were examined in patients who underwent preoperative chemoradiotherapy compared to patients who did not¹⁷. Furthermore, although it has been proposed that increasing the number of lymph nodes harvested might increase the probability of recovering positive lymph nodes¹⁸, the number of patients with positive nodes was similar in both groups in the current study. Persiani et al.¹⁹ was also of the opinion that a low number of lymph nodes harvested during surgery after neoadjuvant chemoradiotherapy does not represent inadequate resection or understaging, rather an increased sensitivity to the treatment.

In theory, ELAPE has the potential to reduce local recurrences and improve survival in low rectal cancer patients with more peritumoral tissue removed. The long-term survival of low rectal cancer patients undergoing ELAPE and APE has been a matter of debate in recent years^{13,16,20}. Klein et al.¹³ reported that there is no evidence indicating that ELAPE yields better survival compared to APE. This population, however, had more early-stage tumors (46 per cent considered to be pT₁₋₂), which might explain why no statistical difference in survival was detected between the two operation types. Shen et al.⁶ has proposed a different view. Specifically, a multicenter study revealed that ELAPE is associated with longer survival

than APE (median OS, 41.5 versus 29.8 months, $P = 0.028$; median DFS: 38.5 versus 29.3 months, $P = 0.027$; local recurrence rate: 3.80 per cent versus 11.5 per cent, $P = 0.027$). In the current study, we showed that ELAPE improved long-term PFS and LRFS for all patients with low rectal cancer compared to APE, which was consistent with the results of Shen et al.⁶. Even though a significant OS was obtained, ELAPE had the added benefit of reducing local recurrences and distant metastases, which facilitates decision-making in selecting the optimal operation type for patients with low rectal cancer.

Further stratified analyses showed patients with pT₃ tumors had better survival outcomes in the ELAPE group than the APE group with comparable neoadjuvant chemoradiotherapy rate [34.5 per cent (10 of 29) versus 21.7 per cent (5 of 23), $P = 0.314$]. Due to insufficient resection range at the surgical waist, APE was associated with a higher risk for positive CRM, which can easily lead to local recurrences. Compared to APE, more peritumoral tissues are removed in patients who undergo ELAPE to avoid the formation of a waist at the anorectal junction, thus reducing the positive CRM rate and improving survival outcomes²¹. In the current study, although the difference in positive CRM rates between the two groups was not significant for all patients, for pT₃, the positive CRM rate for pT₃ in the ELAPE group was significantly lower compared to the APE group [0 versus 13 per cent (3 of 23), $P = 0.045$]. In contrast, complete removal of the mesorectum during the ELAPE procedure reduces the perforation rate during the operation and the incidence of recurrences and metastases²². In addition, with less direct manipulation and squeezing of the tumor during ELAPE, the likelihood of distant metastasis caused by the cancer cells entering the blood is reduced. The importance of resection along the lateral fascial plane of the external anal sphincter-levator muscle is emphasized in the ELAPE procedure in compliance with the precise principle of radical removal²³. Based on our analysis, ELAPE is more suitable for patients with pT₃ rectal cancer.

For patients with positive lymph nodes, ELAPE resulted in an incremental survival benefit in the current study with a higher proportion of patients receiving neoadjuvant chemoradiotherapy. For cases that tumor was difficult to remove, neoadjuvant chemoradiotherapy can downstage the tumor to increase the probability of resection^{24,25}. Even though neoadjuvant chemoradiotherapy is essential in the treatment of advanced rectal cancer, we suggest that the ELAPE might be a crucial method by which to promote survival, as confirmed by multivariate analysis. In the current study patients had a significantly higher 5-year PFS in the ELAPE group than the APE group with or without preoperative neoadjuvant chemoradiotherapy. Seshadri et al.²¹ also reported that ELAPE resulted in better CRM and IOP outcomes when compared with APE, even after neoadjuvant chemoradiotherapy, but concluded that the operation type still plays an important role in long-term survival. Compared with APE, ELAPE removed more tissue to achieve total mesorectal excision, which might have a positive effect on the prognosis of low rectal cancer patients²⁶.

ELAPE has advantages in treating lower rectal cancer compared to APE, but this superiority wasn't reflected in pT₀₋₂ and pT₄ patients in the current study. For pT₁₋₂ tumors, in which cancer cells shallowly infiltrate the intestinal wall, ELAPE might not further improve the prognosis with more tissue removed. For

pT₄ tumors, although our study with its relatively small sample size did not demonstrate significant differences in survival between two groups, we think we cannot ignore the effect of location of the tumor and invasion depth on local recurrence. We showed that in pT₄ tumors the positive CRMs were mostly associated the resection margin of the anterior wall. We speculate that located in the anterior wall of the rectum, pT₄ tumors might invade the prostate or vaginal wall which is associated with local recurrence after resection^{28,29}. Nevertheless, well-designed prospective randomized clinical trials are needed to improve the prognosis of patients with pT₄ low rectal malignant tumors.

This study had the following limitations. First, this was a retrospective study and selection bias was therefore inevitable. The ELAPE group was more likely to receive preoperative neoadjuvant chemoradiotherapy in this study. Then, as indications for anal preservation in low rectal cancer surgery have relaxed, the number of ELAPE and APE cases have correspondingly declined. The sample size of some subgroups was small, and that definitely affected the precision of the estimations in this study. The relatively small number of patients could limit the interpretation of the results. Finally, the postoperative local recurrence rate of this study was relatively high [21.9 per cent (25 of 114)], especially in the APE group [30.4 per cent (14 of 46)]. We considered that the inclusion of advanced tumors suggested by preoperative impact studies and long follow-up time may also account for it, and the small sample size is another reason. Some indicators such as incidence of intraoperative perforation, quality of mesorectal excision were missing.

Conclusion

With similar surgical outcomes, ELAPE significantly improved the long-term survival of low rectal cancer compared to APE, especially for patients with pT₃ and positive lymph nodes. For pT₀₋₂ and pT₄ tumors, there was no evidence that ELAPE was superior in improving survival. At present, how to reduce the local recurrence rate and improve the long-term survival of patients with advanced low rectal cancer has not been established. Large-scale, prospective, randomized controlled trials are clearly needed.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki and was approved by the local Ethics Committee of Beijing Chaoyang Hospital. All patients provided their informed consent for the use of their data in the study (2011- ke - 143).

Consent for publication

Not applicable

Availability of data and materials

Data is available from the corresponding author upon reasonable request

Competing interests

The authors of the article do not have commercial associations (e.g., consultancies, stock ownership, equity interests, patent-licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted article.

Funds

National Natural Science Foundation of China (82070685); National Natural Science Foundation of China (81802353); Project of Beijing Chaoyang Hospital 1351 talents training (CYXZ-2017-09).

Authors' contributions

Study conception and design: ZZ, GW, CY, HZ, ZW, JH

Acquisition of data: HZ, GL, KC, CY

Analysis and interpretation of data: HZ, GL, KC, CY

Drafting of manuscript: HZ, GL, KC

Final approval: ZZ, GW, BZ, ZW, JH

Critical revision: JH, ZW

Acknowledgement

We thank International Science Editing (<http://www.internationalscienceediting.com>) for editing this manuscript.

All authors have read and approved the final version of the manuscript.

References

1. Campos FG, Habr-Gama A, Nahas SC, Perez RO. Abdominoperineal excision: evolution of a centenary operation. *Dis Colon Rectum*, 2012; 55: 844-853. <https://doi.org/10.1097/DCR.0b013e31825ab0f7>.
2. Salerno G, Daniels IR, Brown G. Magnetic resonance imaging of the low rectum: defining the radiological anatomy. *Colorectal Dis*. 2006 Sep;8 Suppl 3:10-3. <https://doi.org/10.1111/j.1463-1318.2006.01063.x>.
3. Salerno G, Chandler I, Wotherspoon A, Thomas K, Moran B, Brown G. Sites of surgical wasting in the abdominoperineal specimen. *Br J Surg*, 2008; 95: 1147-1154. <https://doi.org/10.1002/bjs.6231>.

4. Law WL, Chu KW. Abdominoperineal resection is associated with poor oncological outcome. *Br J Surg*, 2004; 91: 1493-1499. <https://doi.org/10.1002/bjs.4723>.
5. Holm T, Ljung A, Häggmark T, Jurell G, Lagergren J. Extended abdominoperineal resection with gluteus maximus flap reconstruction of the pelvic floor for rectal cancer. *Br J Surg*, 2007; 94: 232-238. <https://doi.org/10.1002/bjs.5489>.
6. Shen Z, Bu Z, Li A, Lu J, Zhu L, Chong CS, et al. Multicenter study of surgical and oncologic outcomes of extra-levator versus conventional abdominoperineal excision for lower rectal cancer. *Eur J Surg Oncol*, 2020; 46: 115-122. <https://doi.org/10.1016/j.ejso.2019.08.017>.
7. Zhou X, Sun T, Xie H, Zhang Y, Zeng H, Fu W. Extralevator abdominoperineal excision for low rectal cancer: a systematic review and meta-analysis of the short-term outcome. *Colorectal Dis*, 2015; 17: 474-481. <https://doi.org/10.1111/codi.12921>.
8. Bianco F, Romano G, Tsarkov P, et al. Extralevator with vs nonextralevator abdominoperineal excision for rectal cancer: the RELAPe randomized controlled trial. *Colorectal Dis*, 2017; 19: 148-157. <https://doi.org/10.1111/codi.13436>.
9. Lehtonen T, Räsänen M, Carpelan-Holmström M, Lepistö A. Oncological outcomes before and after the extralevator abdominoperineal excision era in rectal cancer patients treated with abdominoperineal excision in a single centre, high volume unit. *Colorectal Dis*, 2019; 21: 183-190. <https://doi.org/10.1111/codi.14468>.
10. West NP, Anderin C, Smith KJ, Holm T, Quirke P. Multicentre experience with extralevator abdominoperineal excision for low rectal cancer. *Br J Surg*, 2010; 97: 588-599. <https://doi.org/10.1002/bjs.6916>.
11. Carpelan A, Karvonen J, Varpe P, et al. Extralevator versus standard abdominoperineal excision in locally advanced rectal cancer: a retrospective study with long-term follow-up. *Int J Colorectal Dis*, 2018; 33: 375-381. <https://doi.org/10.1007/s00384-018-2977-y>.
12. Prytz M, Angenete E, Bock D, Haglind E. Extralevator Abdominoperineal Excision for Low Rectal Cancer—Extensive Surgery to Be Used With Discretion Based on 3-Year Local Recurrence Results: A Registry-based, Observational National Cohort Study. *Ann Surg*, 2016; 263: 516-521. <https://doi.org/10.1097/SLA.0000000000001237>.
13. Klein M, Colov E, Gogenur I. Similar long-term overall and progression-free survival after conventional and extralevator abdominoperineal excision—a nationwide study. *Int J Colorectal Dis*, 2016; 31: 1341-1347. <https://doi.org/10.1007/s00384-016-2596-4>.
14. Yu HC, Peng H, He XS, Zhao RS. Comparison of short- and long-term outcomes after extralevator abdominoperineal excision and standard abdominoperineal excision for rectal cancer: a systematic review and meta-analysis. *Int J Colorectal Dis*, 2014; 29: 183-191. <https://doi.org/10.1007/s00384-013-1793-7>.
15. Han JG, Wang ZJ, Gao ZG, Xu HM, Yang ZH, Jin ML. Pelvic floor reconstruction using human acellular dermal matrix after cylindrical abdominoperineal resection. *Dis Colon Rectum*, 2010; 53: 219-223. <https://doi.org/10.1007/DCR.0b013e3181b715b5>.

16. De Nardi P, Summo V, Vignali A, Capretti G. Standard versus extralevator abdominoperineal low rectal cancer excision outcomes: a systematic review and meta-analysis. *Ann Surg Oncol*, 2015; 22: 2997-3006. <https://doi.org/10.1245/s10434-015-4368-8>.
17. Baxter NN, Morris AM, Rothenberger DA, et al. Impact of preoperative radiation for rectal cancer on subsequent lymph node evaluation: a population-based analysis. *Int J Radiat Oncol Biol Phys*, 2005; 61: 426-431. <https://doi.org/10.1016/j.ijrobp.2004.06.259>.
18. Hogan NM, Winter DC. A nodal positivity constant: new perspectives in lymph node evaluation and colorectal cancer. *World J Surg*, 2013; 37: 878-882. <https://doi.org/10.1007/s00268-012-1891-7>.
19. Persiani R, Biondi A, Gambacorta MA, Bertucci Zoccali M, Vecchio FM, Tufo A. Prognostic implications of the lymph node count after neoadjuvant treatment for rectal cancer. *Br J Surg*, 2014; 101: 133-142. <https://doi.org/10.1002/bjs.9341>.
20. Kamali D, Sharpe A, Musbahi A, Reddy A. Oncological and quality of life outcomes following extralevator versus standard abdominoperineal excision for rectal cancer. *Ann R Coll Surg Engl*, 2017; 99: 402-409. <https://doi.org/10.1308/rcsann.2017.0038>.
21. Seshadri RA, West NP, Sundersingh S. A pilot randomized study comparing extralevator with conventional abdominoperineal excision for low rectal cancer after neoadjuvant chemoradiation. *Colorectal Dis*, 2017; 19: 0253-0262. <https://doi.org/10.1111/codi.13726>.
22. Perdawood SK, Lund T. Extralevator versus standard abdominoperineal excision for rectal cancer. *Tech Coloproctol*, 2015; 19: 145-152. <https://doi.org/10.1007/s10151-014-1243-8>.
23. Han JG, Wang ZJ, Wei GH, Gao ZG, Yang Y, Zhao BC. Randomized clinical trial of conventional versus cylindrical abdominoperineal resection for locally advanced lower rectal cancer. *Am J Surg*, 2012; 204: 274-282. <https://doi.org/10.1016/j.amjsurg.2012.05.001>.
24. Gravante G, Miah A, Mann CD, et al. Circumferential resection margins and perineal complications after neoadjuvant long-course chemoradiotherapy followed by extralevator abdominoperineal excision of the rectum: Five years of activity at a single institution. *J Surg Oncol*, 2016; 114: 86-90. <https://doi.org/10.1002/jso.24257>.
25. Horvat N, Carlos Tavares Rocha C, Clemente Oliveira B, Petkovska I, Gollub MJ. MRI of Rectal Cancer: Tumor Staging, Imaging Techniques, and Management. *Radiographics*, 2019; 39: 367-387. <https://doi.org/10.1148/rg.2019180114>.
26. Wu AW, Gu J, Wang J, et al. Results after change of treatment policy for rectal cancer—report from a single hospital in China. *Eur J Surg Oncol*. 2007 Aug; 33:718-723. <https://doi.org/10.1016/j.ejso.2006.12.011>.
27. Nagtegaal ID, Quirke P. What is the role for the circumferential margin in the modern treatment of rectal cancer? *J Clin Oncol*, 2008; 26: 303-312. <https://doi.org/10.1200/JCO.2007.12.7027>.
28. Chan CL, Bokey EL, Chapuis PH, Renwick AA, Dent OF. Local recurrence after curative resection for rectal cancer is associated with anterior position of the tumour. *Br J Surg*, 2006; 93: 105-112. <https://doi.org/10.1002/bjs.5212>.

29. Messenger DE, Cohen Z, Kirsch R, O'Connor BI, Victor JC, Huang H. Favorable pathologic and long-term outcomes from the conventional approach to abdominoperineal resection. *Dis Colon Rectum*. 2011; 54:793–802. <https://doi.org/10.1007/DCR.0b013e318215a1cb>.
30. Stelzner S, Hellmich G, Sims A, et al. Long-term outcome of extralevator abdominoperineal excision (ELAPE) for low rectal cancer. *Int J Colorectal Dis*. 2016 Oct;31(10):1729-1737. Epub 2016 Sep 9. <https://doi.org/10.1007/s00384-016-2637-z>.

Figures

Figure 1

Study flow chart.

Figure 2

Comparison of OS, PFS and LRFS between patients who underwent ELAPE and APE procedure. (a) OS; (b) PFS; (c) LRFS.

Figure 3

Comparison of OS, PFS and LRFS between patients of pT3 who underwent ELAPE and APE procedure. (a) OS; (b) PFS; (c) LRFS.

Figure 4

Comparison of OS, PFS and LRFS between patients of pT0-2 or pT4 who underwent ELAPE and APE procedure. (a) pT0-2: OS; (b) pT0-2: PFS; (c) pT0-2: LRFS; (d) pT4: OS; (e) pT4: PFS; (f) pT4: LRFS.

Figure 5

Comparison of OS, PFS and LRFS between patients of pN+ who underwent ELAPE and APE procedure. (a) OS; (b) PFS; (c) LRFS.

Figure 6

Comparison of OS, PFS and LRFS between patients of pN+ without neoadjuvant chemoradiotherapy or with neoadjuvant chemoradiotherapy who underwent ELAPE and APE procedure. (a) without neoadjuvant chemoradiotherapy: OS; (b) without neoadjuvant chemoradiotherapy: PFS; (c) without neoadjuvant chemoradiotherapy: LRFS; (d) with neoadjuvant chemoradiotherapy: OS; (e) with neoadjuvant chemoradiotherapy: PFS; (f) with neoadjuvant chemoradiotherapy: LRFS.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [SupplementaryTable1.docx](#)
- [SupplementaryTable2.docx](#)
- [SupplementaryTable3.docx](#)
- [SupplementaryTable4.docx](#)
- [SupplementaryTable5.docx](#)
- [SupplementaryTable6.docx](#)