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Laparoscopic extralevator abdominoperineal resection versus laparoscopic abdominoperineal resection for lower rectal cancer: A retrospective comparative study from China

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ABSTRACT

Background: This study was performed to compare the short- and long-term outcomes of laparoscopic extralevator abdominoperineal resection (LELAPR) versus laparoscopic abdominoperineal resection (LAPR) in patients with lower rectal cancer.

Methods: Consecutive patients who underwent LELAPR or LAPR in our unit from September 2009 to December 2015 were retrospectively reviewed. The patients' clinicopathological data and short- and long-term outcomes were compared and analyzed.

Results: Of the 111 patients included in this study, 58 (52%) patients underwent LAPR and 53 (48%) LELAPR. A negative circumferential resection margin was achieved in all the two groups of patients. The LELAPR group had a longer operation time (P = 0.049), more intraoperative blood loss (P = 0.037), shorter hospitalization after surgery (P = 0.002), fewer lymph nodes harvested (P = 0.001), fewer positive lymph nodes (P = 0.002), and a shorter maximum tumor diameter (P < 0.001) compared with the LAPR group. There were also lower rates of intraoperative perforation (P = 0.039) and death (P = 0.013) in the LELAPR group. However, there were no significant differences in the rates of local recurrence (P = 0.144), metastasis (P = 0.111), overall survival (P = 0.404), disease-free survival (P = 0.515), or progression-free survival (P = 0.210) between the two groups. There were no significant differences in postoperative complications including postoperative hernia (P = 0.918), urinary retention (P = 0.579), intestinal obstruction (P = 1.0), and perineal wound complications (P = 0.252).

Conclusions: Compared with LAPR, the LELAPR approach significantly reduced the rate of intraoperative perforation and postoperative death without increasing postoperative complications. LELAPR was beneficial to patients with ulcerative, anterior and advanced lower rectal cancer.

1. Introduction

Extralevator abdominoperineal resection (ELAPR) has been considered to reduce the rate of intraoperative perforation (IOP), circumferential resection margin (CRM) positivity, and even local recurrence (LR) when compared with abdominoperineal resection (APR) [1–3]. This improved performance of ELAPR may result from the absence of the "surgical waist," which is located 3.5–4.2 cm from the anal verge, that remains after APR [4]. However, two nationwide studies [5,6] and one meta-analysis [7] reported comparable results of APR, demonstrating its noninferiority to ELAPR. Thus, no definitive answer has been achieved whether one is superior to the other. Meanwhile, a high-quality meta-analysis of randomized controlled trials proved the safety and efficacy of laparoscopic techniques for treatment of rectal cancer [8]. However, reports of the short- and long-term outcomes of laparoscopic ELAPR (LELAPR) and laparoscopic APR (LAPR) are rare.

Therefore, this study retrospectively compare the short- and long-term outcomes of LELAPR versus LAPR among patients with lower rectal cancer in our unit.

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2. Material and method

2.1. Patients

From September 2009 to December 2015, a total of 111 patients with lower rectal cancer (≤5 cm from the anal verge to the lower margin of the tumor) were treated in our unit. Of these patients, 58 underwent LAPR and 53 underwent LELAPR. All patients were eligible for curative R0 resection by either LELAPR or LAPR. All patients and their families provided written informed consent before surgery. The study has been reported in line with the strengthening the reporting of cohort studies in surgery (STROCSS) criteria [9]. Preoperative colonoscopy and pathological biopsy confirmed lower rectal cancer in all patients. Clinical staging was performed by chest X-ray examination, abdominal ultrasonography, thoracoabdominal computed tomography, and magnetic resonance imaging. Computed tomography and magnetic resonance imaging were repeated after the completion of chemoradiation to evaluate the response to neoadjuvant therapy. Surgery was performed 8 weeks after the completion of chemoradiation. Patients who underwent neoadjuvant therapy received 50.4–54.0 Gy of radiation and 5-FU-based chemotherapy (capecitabine) before surgery. Postoperative chemotherapy (FOLFOX plan) was recommended to all patients with positive lymph nodes as described in the final pathology report. All treatment decisions were ratified by the hospital multidisciplinary team in our unit.

The indications for LELAPR were the same as those for LAPR: a tumor with direct invasion of the anal sphincter and distal rectal tissue in which a safe distal margin was impossible to achieve with a sphincter-preserving technique. Three surgeons from the same group in our unit successfully completed all surgeries together. LELAPR was divided into abdominal and perineal operations. The abdominal procedure was performed according to the principle of total mesorectal excision [10]. The mesorectum was dissociated to the beginning of the levator ani muscles, and the potential gap between the levator ani muscle and rectal mesentery was not opened. The descending colon was then dissociated from the predetermined stoma and cut off. Finally, the end colostomy was formed and the abdomen was closed. The patient was then turned to the prone jackknife position. The anus was sutured first, and the perineal operations were performed as described in the literature [11]. LAPR was performed as described in the literature [12]. All surgical specimens were reviewed by the Pathology Department in our hospital. All pathology reports truthfully recorded the pathological type, tumor differentiation and type, lymph nodes examined, positive lymph nodes, maximum tumor diameter, pTNM, pathologic complete remission (pCR), and CRM positivity. The patients were followed up every 3 months for the first 2 years postoperatively and then every 6 months thereafter. Colonoscopy was performed 1 year postoperatively and then repeated every 3 years if no lesion was found. Data from the last available follow-up visit were also included in the analysis.

2.2. Variables and definitions

The patients' detailed clinicopathological data are shown in Table 1, including gender, age, body mass index, number of neoadjuvant therapy and postoperative chemotherapy sessions, distance to anal verge, American Society of Anesthesiologists physical status, clinical and pathological categories, pathological type, tumor differentiation, and tumor type. The detailed short-term outcomes are shown in Table 2, including the duration of hospitalization after surgery, total operating time, intraoperative blood loss, lymph nodes examined, positive lymph nodes, maximum tumor diameter, IOP rate, pCR rate, and postoperative complications. The postoperative complications included postoperative hernia, urinary retention, intestinal obstruction, and perineal wound complications (PWC). The detailed long-term outcomes are shown in Table 3, including the rate of LR, metastasis, death, overall survival (OS), disease-free survival (DFS), progression-free survival (PFS), loss to follow-up, and follow-up time. OS, DFS, and PFS are also shown in Figs. 1, 2, and 3, respectively.

Lower rectal cancer was defined as rectal cancer with a distance of ≤5 cm from the anal verge to the lower margin of the tumor. Any tumor located < 1 mm from the CRM was defined as positive according to the established consensus [13]. The definition of IOP was tumor perforation under direct vision during surgery or recorded in the surgical record. pCR was defined as the absence of residual invasive tumor tissue in the rectum or regional lymph nodes after neoadjuvant therapy by pathologic evaluation of the surgical samples. Patients with pCR after neoadjuvant therapy were classified as pT0N0M0. PWC mainly included perineal wound infection, dehiscence, breakdown, wound healing problems, and sinus formation.

2.3. Statistics

The statistical analysis was performed using SPSS version 19.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation, and were analyzed using the Independent student's t-test or Mann–Whitney *U* test. Categorical data were analyzing using the chi-square test. Survival analysis was performed using Kaplan–Meier curves, and the log-rank test was used for comparisons. A *p value* of < 0.05 was considered statistically significant for each test.

3. Results

3.1. Clinicopathological data

Gender, age, body mass index, postoperative chemotherapy, distance to anal verge, American Society of Anesthesiologists physical status, clinical and pathological categories, pathological type, tumor differentiation, and tumor type were not significantly different between the two groups, as shown in Table 1. All patients in the LELAPR group underwent neoadjuvant therapy before surgery with statistical significance [53 patients (100%) vs. 10 patients (17%), respectively P < 0.001] (Table 1).

3.2. Short-term outcomes

In terms of perioperative variables, the total operating time in the LELAPR group was slightly longer than that in the LAPR group [256.59 ± 47.52 (244–270) vs. 242.17 ± 62.98 (226–259) min, respectively; P = 0.049] (Table 2). The LELAPR group also had more intraoperative blood loss than the LAPR group [86.60 ± 57.11 (71-102) vs. 72.33 ± 56.10 (58-87) ml, respectively; P = 0.037] (Table 2). However, the LELAPR group had fewer lymph nodes examined [11.47 ± 6.98 (10-13) vs. 14.95 ± 6.77 (13-17), respectively; P = 0.001] and fewer positive lymph nodes [0.75 ± 1.81 (0-1) vs. 3.03 ± 5.14 (2-4),respectively; P = 0.002] (Table 2). The maximum tumor diameter was shorter in the LELAPR than LAPR group [2.51 ± 0.85 (2-3) vs. 3.78 ± 1.45 (3-4) cm, respectively; P < 0.001] (Table 2). In terms of postoperative variables, no postoperative hospital death occurred in either group. Postoperative hernia formation, postoperative urinary retention, intestinal obstruction, and PWC were all comparable between the two groups. However, the postoperative hospital stay was shorter in the LELAPR than LAPR group [9.53 ± 4.49 (8-11) vs. 11.67 ± 4.89 (10-13) days, respectively; P = 0.002] (Table 2). In terms of oncological variables, a negative CRM was obtained in all patients in both groups. The IOP rate was lower in the LELAPR than LAPR group [2 (4%) vs. 9 (16%) patients, respectively; P = 0.039] (Table 2). Moreover, the rate of pCR after neoadjuvant therapy was not significantly different between the LELAPR and LAPR groups [7 (13%) vs. 0 (0%) patients, respectively; P = 0.503] (Table 2).

Table 1
Patients clinicopathological data.

Characteristics	LELAPR (53)	LAPR (58)	*p* values
Gender (n)			0.710
Male	32	33	
Female	21	25	
Age (years)	60.26 ± 7.96 (58–62)	57.35 ± 11.09 (54–60)	0.112
Body mass index (kg/m^2)	25.46 ± 3.13 (24–26)	24.34 ± 3.25 (23–25)	0.067
Neoadjuvant therapy (n)	53/53	10/58	*0.000*[a]
Postoperative chemotherapy (n)	20/53	25/58	0.565
Distance to anal verge (cm)	3.60 ± 1.12 (3–4)	3.22 ± 1.06 (3-4)	0.069
American Society of Anesthesiologists score (n)			0.340
I	0/53	6/58	
II	48/53	45/58	
III	5/53	7/58	
IV ~ V	0/53	0/58	
Clinical tumor (T) category			0.205
1	3/53	2/58	
2	23/53	20/58	
3	20/53	25/58	
4	7/53	11/58	
Clinical tumor (N) category			0.416
0	25/53	21/58	
1	16/53	24/58	
2	12/53	13/58	
Pathological tumor (T) category			0.055
0	7/53	0/58	
1	1/53	1/58	
2	19/53	19/58	
3	17/53	26/58	
4	9/53	12/58	
Pathological node (N) category			0.276
0	33/53	31/58	
1	11/53	12/58	
2	9/53	15/58	
Pathological type (n)			0.339
Adenocarcinoma	53/53	57/58	
Mucinous carcinoma	0/53	1/58	
Tumor differentiation (n)			0.432
Well	4/53	2/58	
Moderate	44/53	44/58	
Moderate-poor	4/53	7/58	
Poor	1/53	5/58	
Tumor type (n)			0.087
Ulcer	47/53	46/58	
Uplift	4/53	11/58	
Ulcer- uplift	2/53	1/58	

LELAPR Laparoscopic extralevator abdominoperineal resection, LAPR Laparoscopic abdominoperineal resection.
p values of < 0.05 are considered statistically significant.
[a] Chi-square test.

Table 2
Comparison of short-term outcomes in lower rectal cancer.

Characteristics	LELAPR(53)	LAPR(58)	*p* values
Hospitalization day after surgery (days)	9.53 ± 4.49 (8–11)	11.67 ± 4.89 (10–13)	*0.002*[b]
Total operating time (min)	256.59 ± 47.52 (244–270)	242.17 ± 62.98 (226–259)	*0.049*[b]
Intraoperative blood loss (ml)	86.60 ± 57.11 (71–102)	72.33 ± 56.10 (58–87)	*0.037*[b]
Lymph nodes examined (n)	11.47 ± 6.98 (10–13)	14.95 ± 6.77 (13–17)	*0.001*[b]
Positive lymph nodes (n)	0.75 ± 1.81 (0–1)	3.03 ± 5.14 (2–4)	*0.002*[b]
Maximum diameter of tumor (cm)	2.51 ± 0.85 (2–3)	3.78 ± 1.45 (3–4)	*0.000*[b]
Intraoperative perforation (n)	2/53	9/58	*0.039*[a]
pCR (n)	7/53	0/10	0.503[a]
Postoperative complications			
Postoperative hernia (n)	3/53	2/58	0.918[a]
Urinary retention (n)	3/53	6/58	0.579[a]
Perineal wound complication (n)	7/53	3/58	0.252[a]
Intestinal obstruction (n)	3/53	4/58	1.000[a]

pCR Pathologic complete response, *LELAPR* Laparoscopic extralevator abdominoperineal resection, *LAPR* Laparoscopic abdominoperineal resection.
[a] Chi-square test.
[b] Mann-Whitney U tests.

Table 3
Comparison of long-term outcomes in lower rectal cancer.

Characteristics	LELAPR(53)	LAPR(58)	*p* values
LR (n)	3/52	8/56	0.144[a]
Metastasis (n)	6/52	13/56	0.111[a]
Death(n)	5/52	16/56	*0.013*[a]
Follow-up time (months)	41.03 ± 9.06 (39–44)	62.27 ± 21.13 (57–68)	*0.000*[b]
Loss to follow-up (n)	1/53	2/58	1.000[a]

LR Local recurrence, *LELAPR* Laparoscopic extralevator abdominoperineal resection, *LAPR* Laparoscopic abdominoperineal resection.
p values of < 0.05 are considered statistically significant.
[a] Chi-square test.
[b] Mann-Whitney U tests.

3.3. Long-term outcomes

With respect to long-term outcomes, although one and two patients in the LELAPR and LAPR groups were lost to follow-up, respectively, the difference between the groups was not significant (P = 1.0) (Table 3). The mean follow-up time was significantly shorter in the LELAPR than LAPR group [41.03 ± 9.06 (39-44) vs. 62.27 ± 21.13 (57-68) months, respectively; P < 0.001] (Table 3). The LELAPR and LAPR groups showed no significant differences in the rates of LR [3 (6%) vs. 8 (14%) patients, respectively; P = 0.144] and metastasis [6 (12%) vs. 13 (23%) patients, respectively; P = 0.111] (Table 3). In the LELAPR group, three patients with LR all had PWC, including two patients with perineal wound infection and one patient with delayed wound healing. In the LAPR group, five patients developed IOP, two developed perineal wound infection, and one developed simultaneous IOP and perineal wound infection. Additionally, in the LELAPR group, two patients had lung metastasis, one had brain metastasis, one had liver and lung metastasis, and two had bone and lung metastasis. In the LAPR group, one patient had LR and uterine metastasis; one had bone metastasis; one had liver metastasis; one had bone, lung, and liver metastasis; five had lung metastasis; two had uterine metastasis; and two had liver and lung metastasis. The OS, DFS, and PFS showed no significant differences between the two groups (Figs. 1–3, respectively). The mortality rate was significantly lower in the LELAPR than LAPR group [5 (10%) vs. 16 (29%) patients, respectively; P = 0.013] (Table 3). During follow-up, 16 patients in the LAPR group died of LR or metastasis. In the LELAPR group, two patients died of LR, one died of metastasis, and two died of other diseases (complications of fracture and renal failure). Even after excluding the patients who died in other diseases in the LELAPR group, the final result did not change. The mean length of OS was 87 months in the LELAPR group and 56 months in the LAPR group (P = 0.404, log-rank test) (Fig. 1). The mean length of DFS was 84 months in the LELAPR group and 53 months in the LAPR group (P = 0.515, log-rank test) (Fig. 2). The mean length of PFS was 77 months in the LELAPR group and 51 months in the LAPR group (P = 0.210, log-rank test) (Fig. 3).

To eliminate the effect of neoadjuvant therapy, we analyzed 63 patents (1 patient was lost to follow-up in the LAPR group) who underwent neoadjuvant therapy alone (53 in LELAPR group vs. 10 in LAPR group). Apart from the significantly lower mortality rate in the LELAPR than LAPR group [5 (9%) vs. 4 (44%) patients, respectively; P = 0.021], no significant differences were found in any other short- or long-term outcomes.

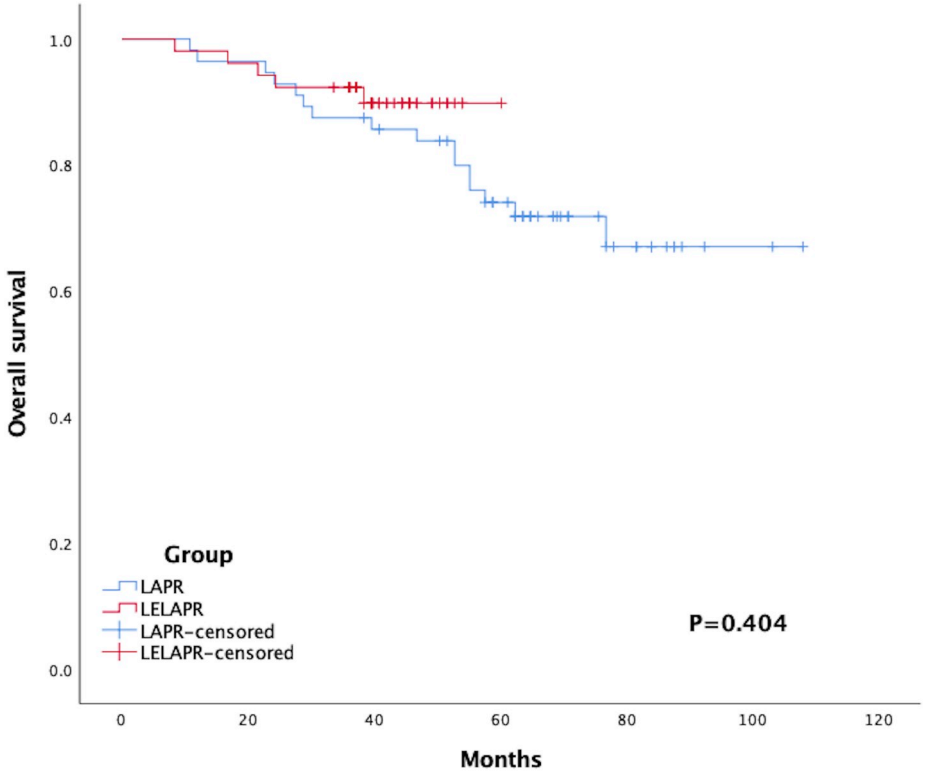

Fig. 1. Kaplan-Meier curves showing the overall survival after extralevator abdominoperineal and abdominoperineal resection under laparoscopic (P = 0.404).

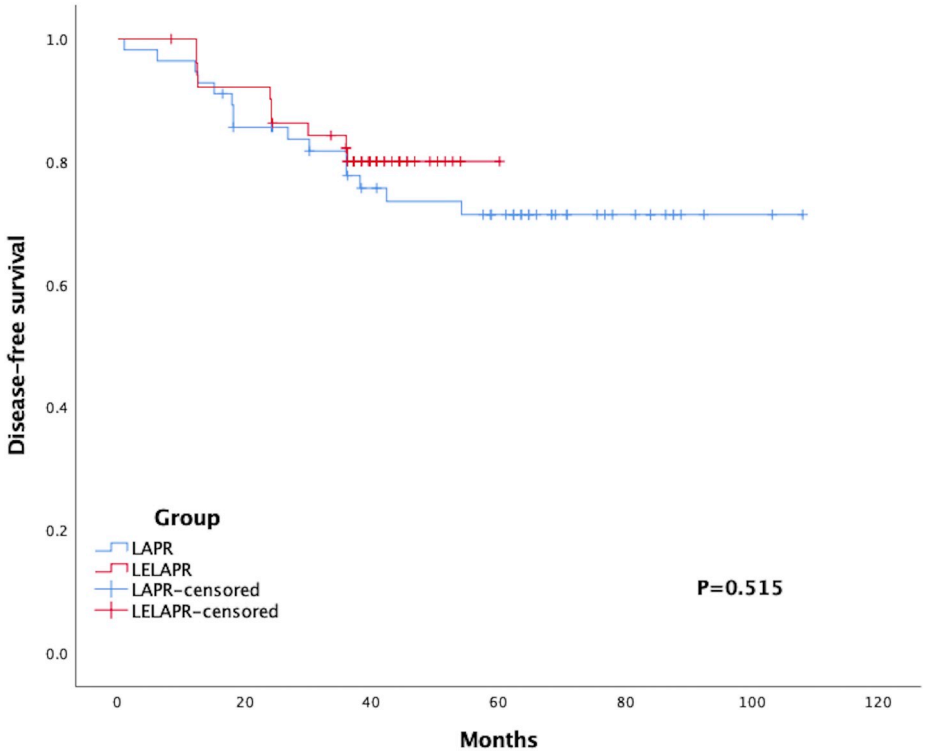

Fig. 2. Kaplan-Meier curves showing the disease-free survival after extralevator abdominoperineal and abdominoperineal resection under laparoscopic (P = 0.515).

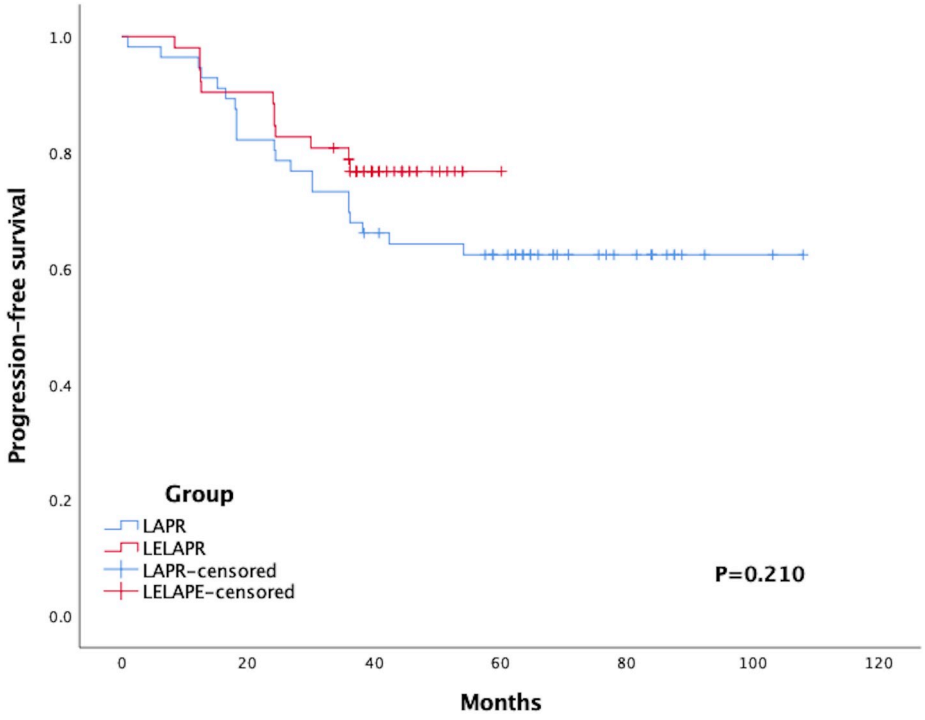

Fig. 3. Kaplan-Meier curves showing the progression-free survival after extralevator abdominoperineal and abdominoperineal resection under laparoscopic (P = 0.210).

4. Discussion

The present study showed that compared with LAPR, LELAPR was associated with a shorter postoperative hospital stay, fewer lymph nodes examined, fewer positive lymph nodes, and a shorter maximum tumor diameter but a longer total operation time and more blood loss. The present study also showed that LELAPR had advantages over LAPR in terms of the LR rate, pCR rate, metastasis, OS, DFS, and PFS, although the differences did not reach statistical significance. Although the postoperative complication rate was higher in the LELAPR group, the difference was not significant. Our most important finding was that LELAPR obviously reduced the IOP rate and mortality during follow-up compared with LAPR.

The increased operation time in the LELAPR group may be

associated with patient repositioning (to the prone jackknife position) after abdominal surgery, which has been proven to increase the operation time in previous studies [2,14]. The increased intraoperative blood loss was not unexpected because the extensive resection during the perineal operation undoubtedly increased the blood loss in the LELAPR group. However, our results regarding the intraoperative blood loss are inconsistent with four previous studies [1,2,11,14]. The selection of surgical methods (open or laparoscopic) might have also impacted the amount of blood loss in those four studies. The shorter hospital stay after surgery was consistent with a study by Kipling [15] and was partly due to the benefit obtained from our increased proficiency in laparoscopy and application of the concept of enhanced recovery after surgery in the perioperative period in our unit. Interestingly, the higher rate of PWC did not lead to longer hospitalization after surgery, which is similar to previous reports [1,11,16]. The numbers of lymph nodes examined and positive lymph nodes, as well as the maximum tumor diameter, were lower in the LELAPR group. The most important reason for this may be partly due to neoadjuvant therapy, which may have decreased the above variables. Neoadjuvant therapy can lead to downstaging of the tumor and should not be ignored under any condition. pCR was obtained after neoadjuvant therapy in 11.1% of patients in the LELAPR group, which is similar to the rate of 10.3% reported in a single UK tertiary center [17] and further confirms the influence of neoadjuvant therapy.

With respect to postoperative complications, besides the similar incidence of postoperative hernia [3 (6%) vs. 2 (3%) patients in LELAPR vs. LAPR, respectively; P = 0.918] and intestinal obstruction [3 (6%) vs. 4 (7%) patients in LELAPR vs. LAPR, respectively; P = 1.0], the incidence of postoperative urinary retention decreased from 10% to 6% in the LELAPR group. The rate of PWC in the LELAPR group was twice that in the LAPR group (13% vs. 5%), which is consistent with four previous studies [1,5,18,19]. Primary closure without a flap or biological mesh to reconstruct the pelvic floor was performed in both groups of the present study. In contrast, Stelzner et al. [20] reported a lower rate of PWC in ELAPR than APR (17% vs. 37%). Shen [2], Han [11], and Habr-Gama [12] also successively demonstrated the superiority of ELAPR over APR in terms of the PWC rate. All four of the above-mentioned studies attributed these favorable results to the materials used in reconstruction of the pelvic floor. Notably, however, there is insufficient evidence to recommend one particular method of perineal closure after ELAPR. Moreover, the small sample sizes in their respective studies using flaps, biological mesh, or other materials to reconstruct the perineal defect after ELAPR may lack external validity to some degree. The higher PWC rate in this study may have been partly due to the performance of LELAPR itself and the administration of neoadjuvant therapy and postoperative chemotherapy. One nationwide study [18] demonstrated that neoadjuvant therapy and LELAPR were significant factors for predicting the rate of PWC. From an anatomical perspective, LAPR involves removing of the structure of the mesorectum. LELAPR expands the scope of resection on the basis of LAPR; therefore, the latter undoubtedly has a longer operation time, more blood loss, and ultimately a larger perineal defect, which could result in a higher PWC rate. A recent report also described increased PWC when neoadjuvant therapy was used regardless of the use of APR or ELAPR [21]. Unfortunately, 10 patients with PWC in both groups of our study had all received neoadjuvant therapy. Moreover, 9 of 10 patients (3 in the LAPR group and 6 in the LELAPR group) also underwent postoperative chemotherapy, which may have further also contributed to PWC. Although no significant differences were found in this study and few reports in the literature have focused on postoperative chemotherapy, this issue deserves further discussion.

The rates of CRM positivity and IOP were also notable in this study. To the best of our knowledge, this is the first study to show that no patients in either group had CRM positivity. The IOP rate was clearly lower in the LELAPR than LAPR group (4% vs. 16%). This result was in line with our expectation and is consistent with three original studies [1,2,14]. Ionut Negoi et al. [22] recently performed a meta-analysis of 11 comparative studies and demonstrated that ELAPR significantly reduced the IOP rate, with no benefits regarding the rates of CRM positivity or LR. The identification of anatomical landmarks was important in LELAPR, especially perineal operations. A recent anatomic dissection study [23] emphasized that clear identification of pelvic anatomic landmarks during surgery might be useful for both achieving CRM negativity and preserving urogenital function. The intraoperative separation and dissection in LELAPR is performed according to the “two-plane method.” The plane of the mesorectum is separated in the abdominal operation and the perineum is separated along the lateral plane of the levator ani muscle, which jointly guarantee clearer visualization of the operation plane and anatomy, eventually reducing the rates of CRM positivity, IOP, and iatrogenic injury. Another reason for the lower IOP rate in LELAPR may lie in the historical change in the surgical position (from lithotomy to prone jackknife) during the perineal operation. This can provide excellent exposure of the perineal structures and better visualization for the operator, therefore further guaranteeing the ability to perform the operation along the anatomical level and reducing the IOP rate. Moreover, with respect to the perforation sites, most of the perforations in two groups were located in the anterior region (10/11), which is similar to the findings of three previous studies [1,17,24]. Interestingly, the tumor type and pTNM of the 11 patients were ulcerative and advanced (T3-4 and N1-2), respectively. Therefore, LELAPR may be more suitable for the ulcerative, anterior, advanced lower rectal cancer.

With respect to long-term variables, lower rectal cancer has been shown to have high rates of CRM positivity and IOP and a poor prognosis [25,26]. Septic complications of the perineal wound are also reportedly associated with a higher rate of LR [27]. The LR rate was significantly lower after LELAPR than LAPR in our study (6% vs. 14%), although the difference was not significant. LR rates of 0%–7% after ELAPR have been reported in previous studies [2,3,6,10,11,13,18,19], and some studies even showed significantly different rates of LR after APR (15%–32%) [2,10,11,13]. Among our 11 patients with relapse (3 in the LELAPR group and 8 in the LAPR group), none of the 3 patients in the LELAPR group developed IOP or PWC; however, among the 8 patients in the LAPR group, 5 developed IOP, 2 developed PWC, and 1 developed both PWC and IOP simultaneously. This may have resulted in the poorer prognosis in the LAPR group. Only two studies to date [12,14] have successively reported totally different results in terms of the mortality rate during follow-up, but they had small simple sizes without any discussion. Our study showed an obviously lower mortality rate (10%) in the LELAPR group regardless of the effect of neoadjuvant therapy, which is consistent with the study by Habr-Gama [12]. Through further analysis of the LAPR group, we found that the pTNM of 14 patients who died and had not received neoadjuvant therapy had advanced tumors (T3 or T4) and that another 2 patients who died had not received postoperative chemotherapy although they had positive lymph nodes. In contrast, all patients who died in the LELAPR group had received neoadjuvant therapy and postoperative chemotherapy. Therefore, the neoadjuvant therapy and postoperative chemotherapy may have decreased the mortality rate in the long term as well as improved the short-term outcomes mentioned above. Moreover, among the 63 patients who underwent neoadjuvant therapy alone (53 in the LELAPR group and 10 in the LAPR group), the mortality rate decreased from 44% to 9% after surgery, further demonstrating the superiority of LELAPR over LAPR. In addition, the lower mortality rate in the LELAPR group may have also been due to the relatively short follow-up compared with the LAPR group. Finally, this study also revealed no difference in OS, DFS, or PFS between the two groups. Similar results were also reported in one nationwide study in Denmark [28], one study in Finland [19], and two studies in China [2,11].

Two main limitations of this study should be considered. First, despite the comparison of 63 patients (53 LELAPR vs. 10 LAPR) who underwent neoadjuvant therapy alone, all patients in the LELAPR group

underwent neoadjuvant therapy, and this could have affected the results as mentioned above. However, this is also an improvement of the guidelines for rectal cancer , which we can't change, but facing. By balancing the role of neoadjuvant therapy, a prospective study of LELAPR and LAPR in our unit was ongoing. Second, although the mean follow-up time reached 41 months in the LELAPR group, a difference was still present between the two study groups at the 62-month follow-up. Therefore, longer-term survival in the LELAPR group should be assessed in future studies.

5. Conclusions

Compared with LAPR, the LELAPR approach significantly reduced the rate of intraoperative perforation and postoperative death without increasing postoperative complications. Furthermore, LELAPR was beneficial for ulcerative, anterior, advanced lower rectal cancer.

Conflicts of interest

All authors declare that there is no conflict of interest.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Data statement

All data included in this study are available upon request by contacting with the corresponding author (E-mail: cuiming@bjmu.edu.cn).

Declaration of interest

None.

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Ethical approval

This study was approved by the Medical Ethics Committee of Peking University Cancer Hospital (Number:2016KT40) and registered in Chinese Clinical Trial Registry (ChiCTR1900023417).

Research registration Unique Identifying number (UIN)

1. Name of the registry:

   Chinese Clinical Trial Registry.

2. Unique Identifying number or registration ID:

   ChiCTR1900023417.

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Author contribution

Xiangqian Su and Ming Cui contributed to study conception and design, Maoxing Liu, Fei Tan and Kai Xu contributed to acquisition of data, Zhendan Yao, Nan Zhang and Hong Yang contributed to analysis and interpretation of data, Xinyu Qi and Maoxing Liu contributed to drafting of manuscript, Jiadi Xing and Chenghai Zhang contributed to critical revision.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijsu.2019.09.010.

References

[1] N.P. West, C. Anderin, K.J. Smith, T. Holm, P. Quirke, Multicentre experience with extralevator abdominoperineal excision for low rectal cancer, Br. J. Surg. 97 (2010) 588–599 https://doi.org/10.1002/bjs.6916.

[2] Z. Shen, Y. Ye, X. Zhang, Q. Xie, M. Yin, X. Yang, K. Jiang, B. Liang, S. Wang, Prospective controlled study of the safety and oncological outcomes of ELAPE procure with definitive anatomic landmarks versus conventional APE for lower rectal cancer, Eur. J. Cancer. 41 (2015) 472–477 https://doi.org/10.1016/j.ejso.2015.01.017.

[3] G. Neşşar, A.E. Demirbağ, B. Celep, O.H. Elbir, C. Kayaalp, Extralevator abdominoperineal excision versus conventional surgery for low rectal cancer: a single surgeon experience, Ulusal. Cerrahi. Derg. 32 (2016) 244–247 https://doi.org/10.5152/UCD.2016.3251.

[4] G. Salerno, I. Chandler, A. Wotherspoon, K. Thomas, B. Moran, G. Brown, Sites of surgical wasting in the abdominoperineal specimen, Br. J. Surg. 9 (2008) 1147–1154 https://doi.org/10.1002/bjs.6231.

[5] M. Prytz, E. Angenete, J. Ekelund, E. Haglind, Extralevator abdominoperineal excision (ELAPE) for rectal cancer—short-term results from the Swedish Colorectal Cancer Registry. Selective use of ELAPE warranted, Int. J. Colorectal. Dis. 29 (2014) 981–987 https://doi.org/10.1007/s00384-014-1932-9.

[6] H. Ortiz, M.A. Ciga, P. Armendariz, E. Kreisler, A. Codina-Cazador, E. Gomez-Barbadillo, E. Garcia-Granero, J.V. Roig, S. Biondo, Multicentre propensity score-matched analysis of conventional versus extended abdominoperineal excision for low rectal cancer, Br. J. Surg. 101 (2014) 874–882 https://doi.org/10.1002/bjs.9522.

[7] X. Zhou, T. Sun, H. Xie, Y. Zhang, H. Zeng, W. Fu, Extralevator abdominoperineal excision for low rectal cancer: a systematic review and meta-analysis of the short-term outcome, Colorectal. Dis. 17 (2015) 474–481 https://doi.org/10.1111/codi.12921.

[8] F.W. Zhang, Z.Y. Zhou, H.L. Wang, J.X. Zhang, B.S. Di, W.H. Huang, K.H. Yang, Laparoscopic versus open surgery for rectal cancer: a systematic review and meta-analysis of randomized controlled trials, Asian. Pac. J. Cancer. Prev. 15 (2014) 9985–9996 http://doi.org/10.7314/APJCP.2014.15.22.9985.

[9] R.A. Agha, M.R. Borrelli, M. Vella-Baldacchino, R. Thavayogan, D.P. Orgill, The STROCSS statement: strengthening the reporting of cohort studies in surgery, Int. J. Surg. 46 (2017) 198–202.

[10] T. Holm, A. Ljung, T. Häggmark, G. Jurell, J. Lagergren, Extended abdominoperineal resection with gluteus maximus flap reconstruction of the pelvic floor for rectal cancer, Br. J. Surg. 94 (2007) 232–238 https://doi.org/10.1002/bjs.5489.

[11] J.G. Han, Z.J. Wang, G.H. Wei, Z.G. Gao, Y. Yang, B.C. Zhao, Randomized clinical

trial of conventional versus cylindrical abdominoperineal resection for locally advanced lower rectal cancer, Am. J. Surg. 204 (2012) 274–282 https://doi.org/10.1016/j.amjsurg.2012.05.001.

[12] A. Habr-Gama, G.P. São Julião, A. Mattacheo, L.F. de Campos-Lobato, E. Aleman, B.B. Vailati, J. Gama-Rodrigues, R.O. Perez, Extralevator abdominal perineal excision versus standard abdominal perineal excision: impact on quality of the resected specimen and postoperative morbidity, World J. Surg. 41 (2017) 2160–2167 https://doi.org/10.1007/s00268-017-3963-1.

[13] I.J. Adam, M.O. Mohamdee, I.G. Martin, N. Scott, P.J. Finan, D. Johnston, M.F. Dixon, P. Quirke, Role of circumferential margin involvement in the local recurrence of rectal cancer, Lancet. 344 (1994) 707–711 https://doi.org/10.1016/S0140-6736(94)92206-3.

[14] Y.L. Wang, Y. Dai, J.B. Jiang, H.Y. Yuan, S.Y. Hu, Application of laparoscopic extralevator abdominoperineal excision in locally advanced low rectal, Chin. Med. J (Engl). 128 (2015) 1340–1345 https://doi.org/10.4103/0366-6999.156779.

[15] S.L. Kipling, K. Young, J.D. Foster, N.J. Smart, A.E. Hunter, E. Cooper, N.K. Francis, Laparoscopic extralevator abdominoperineal excision of the rectum: short-term outcomes of a prospective case series, Tech. Coloproctol. 18 (2014) 445–451 https://doi.org/10.1007/s10151-013-1071-2.

[16] M. Klein, A. Fischer, J. Rosenberg, I. Gögenur, Extralevatory abdominoperineal excision (ELAPE) does not result in reduced rate of tumour perforation or rate of positive circumferential resection margin, Ann. Surg. 261 (2015) 933–938 https://doi.org/10.1097/SLA.0000000000000910.

[17] A. Hussain, F. Mahmood, A.D.W. Torrance, H. Clarke, C. Howitt, R. Dawson, Oncological outcomes of abdominoperineal resection for the treatment of low rectal cancer: a retrospective review of a single UK tertiary centre experience, Ann. Med. Surg (Lond). 34 (2018) 28–33 https://doi.org/10.1016/j.amsu.2018.06.007.

[18] E.P. Colov, M. Klein, I. Gögenur, Wound complications and perineal pain after extralevator versus standard abdominoperineal excision: a nationwide study, Dis. Colon. Rectum. 59 (2016) 813–821 https://doi.org/10.1097/DCR.0000000000000639.

[19] A. Carpelan, J. Karvonen, P. Varpe, A. Rantala, A. Kaljonen, J. Grönroos, H. Huhtinen, Extralevator versus standard abdominoperineal excision in locally advanced rectal cancer: a retrospective study with long-term follow-up, Int. J. Colorectal. Dis. 33 (2018) 375–381 https://doi.org/10.1007/s00384-018-2977-y.

[20] S. Stelzner, G. Hellmich, A. Sims, T. Kittner, E. Puffer, J. Zimmer, D. Bleyl, H. Witzigmann, Long-term outcome of extralevator abdominoperineal excision (ELAPE) for low rectal cancer, Int. J. Colorectal. Dis. 31 (2016) 1729–1737 https://doi.org/10.1007/s00384-016-2637-z.

[21] J.D. Foster, S. Tou, N.J. Curtis, N.J. Smart, A. Acheson, C. Maxwell-Armstrong, A. Watts, B. Singh, N.K. Francis, Closure of the perineal defect after abdominoperineal excision for rectal adenocarcinoma - ACPGBI position statement, Colorectal. Dis. 20 (2018) 5–23 https://doi.org/10.1111/codi.14348.

[22] I. Negoi, S. Hostiuc, S. Paun, R.I. Negoi, M. Beuran, Extralevator vs conventional abdominoperineal resection for rectal cancer—a systematic review and meta-analysis, Am. J. Surg. 212 (2016) 511–526 https://doi.org/10.1016/j.amjsurg.2016.02.022.

[23] S. Stelzner, T. Holm, B.J. Moran, H. Witzigmann, D. Zorenkov, T. Wedel, Deep pelvic anatomy revisited for a description of crucial steps in extralevator abdominoperineal excision for rectal cancer, Dis. Colon. Rectum. 54 (2011) 947–957 https://doi.org/10.1097/DCR.0b013e31821c4bac.

[24] J.G. Han, Z.J. Wang, Q. Qian, Y. Dai, Z.Q. Zhang, J.S. Yang, F. Li, X.B. Li, A prospective multicenter clinical study of extralevator abdominoperineal resection for locally advanced low rectal cancer, Dis. Colon. Rectum. 57 (2014) 1333–1340 https://doi.org/10.1097/DCR.0000000000000235.

[25] I.D. Nagtegaal, C.J. van de Velde, C.A. Marijnen, J.H. van Krieken, P. Quirke, Low rectal cancer: a call for a change of approach in abdominoperineal resection, J. Clin. Oncol. 23 (2005) 9257–9264 https://doi.org/10.1200/JCO.2005.02.9231.

[26] M. den Dulk, C.A. Marijnen, H. Putter, H.J. Rutten, G.L. Beets, T. Wiggers, I.D. Nagtegaal, C.J. van de Velde, Risk factors for adverse outcome in patients with rectal cancer treated with an abdominoperineal resection in the total mesorectal excision trial, Ann. Surg. 246 (2007) 83–90 https://doi.org/10.1097/01.sla.0000259432.29056.9d.

[27] K.M. Bullard, J.L. Trudel, N.N. Baxter, D.A. Rothenberger, Primary perineal wound closure after preoperative radiotherapy and abdominoperineal resection has a high incidence of wound failure, Dis. Colon. Rectum. 48 (2005) 438–443 https://doi.org/10.1007/s10350-004-0827-1.

[28] M. Klein, E. Colov, I. Gögenur, Similar long-term overall and disease-free survival after conventional and extralevator abdominoperineal excision—a nationwide study, Int. J. Colorectal. Dis. 31 (2016) 1341–1347 https://doi.org/10.1007/s00384-016-2596-4.