

Comparison of short- and long-term outcomes after extralevator abdominoperineal excision and standard abdominoperineal excision for rectal cancer: a systematic review and meta-analysis

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Abstract

Purpose Whether the introduction of extralevator abdominoperineal excision (ELAPE) improves survival and safety remains controversial. We conducted a systematic review and meta-analysis of all comparative studies to define the efficacy and safety of ELAPE and standard abdominoperineal excision (APE).

Materials and methods A search for all major databases and relevant journals from inception to July 2013 without restriction on languages or regions was performed. Outcome measures were the oncological parameters of circumferential resection margin (CRM) involvement, intraoperative bowel perforation (IOP), and local recurrence, as well as other parameters of blood loss, operative time, length of hospitalization, and postoperative complication. The test of heterogeneity was performed with the Q statistic.

Results A total of 949 patients were included in the meta-analysis. Oncological pooled estimates of intraoperative bowel perforation rate (RR 0.34; 95 % CI 0.21–0.54; $P < 0.00001$), CRM involvement (RR 0.44; 95 % CI 0.34–0.56; $P < 0.00001$), and local recurrence (RR 0.32; 95 % CI 0.14–0.74; $P = 0.008$) all showed outcomes that were significantly lower in ELAPE than in APE. A similar incidence of postoperative complication was attributed to both groups, including overall complication (RR 0.93; 95 % CI 0.66–1.32; $P = 0.69$), perineal wound complication (RR 0.72; 95 % CI 0.33–1.55;

$P = 0.39$), and urinary dysfunction (RR 1.53; 95 % CI 0.88–2.67; $P = 0.13$).

Conclusion ELAPE has a lower intraoperative bowel perforation rate, positive CRM rate, and local recurrence rate than APE. There is evidence that in selected low rectal cancer patients, ELAPE is a more efficient and equally safe option to replace APE. Due to the inherent limitations of the present study, future randomized controlled trials will be useful to confirm this conclusion.

Keyword Extralevator abdominoperineal excision · Circumferential resection margin · Local recurrence · Intraoperative bowel perforation · Complication

Introduction

Surgical removal of the rectal tumor is the only curative therapeutic approach, often in combination with chemoradiotherapy or radiotherapy [1]. Abdominoperineal excision (APE) is still commonly required for patients with T3/T4 low rectal cancer. A number of studies have shown that outcomes in terms of local recurrence and survival are worse after APE than after low anterior resection (LAR) [2–4]. Standard APE produces a specimen with a “waist”, while an extended posterior perineal approach in APE, a more radical approach closely mirroring the original Miles operation [5], has recently been introduced to achieve a cylindrical specimen and less risk of circumferential resection margin (CRM) involvement, and by inference of local recurrence of the tumor in lower rectum [6]. Since then, the use of extralevator APE (ELAPE) had been spread because of its benefits in terms of postoperative recovery and long-term morbidity [7–10]. There have been some randomized trials and retrospective studies comparing standard APE with ELAPE on short- and long-term outcomes, but no definitive conclusions

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regarding objective differences in outcomes have been reached. We therefore performed a systematic review and meta-analysis of the available published literature to compare the outcomes of the two approaches.

Methods

Literature search

A literature search of MEDLINE, EMBASE, and the Cochrane Library was performed on all the relevant studies published between 2007 and 2013. We choose to start in 2007 because ELAPE was expected to be implemented in most colorectal units around that time. No language or region restrictions were applied to avoid publication bias. The following keywords were used in searching: “(extralevator abdominoperineal OR extralevator abdominoperineal OR abdominosacral amputation OR cylindrical abdominoperineal OR extended abdominoperineal OR abdominoperineal prone position) [Title/Abstract].” Articles were also identified using the “related articles” function. Moreover, we performed a manual search of references lists of retrieved articles and published reviews to search for additional related studies. The latest date of this search was 17 July 2013.

Inclusion criteria

Studies selected from the initial search were subsequently screened for eligibility with the following criteria:

1. Low rectal cancer determined by preoperative magnetic resonance imaging or endorectal ultrasonography examination or a low tumor is fixed or tethered at rectal examination.
2. Studies reported for perineal flap reconstructions in cylindrical procedure.
3. Clear documentation of the surgical technique as ELAPE and conventional APE.
4. Evaluation of at least one of the outcomes of interest mentioned below.

Exclusion criteria

The following exclusion criteria were used: The inclusion criteria were not met; with operation contraindication; and nonhuman studies, experimental trials, review articles, editorials, letters and case reports, and articles not reporting the outcomes of interest.

The data sets of two studies [11] overlapped and were duplicated; only the most recent and high-quality information was included. All identified studies were reviewed independently for eligibility by two authors.

Data extraction

Two authors independently extracted data from the included studies, and data were cross-checked to reach a consensus. The following variables were extracted from each study: first author, year of publication, institution, study design, inclusion and exclusion criteria, matching criteria, sample size (cases and controls or cohort size), and outcomes of interest. In all cases of missing or incomplete data, the primary authors were contacted for original information, but none provided any additional information.

Outcomes of interest and definitions

The following outcomes were used to compare APE and ELAPE:

1. Perioperative variables: operating time and estimated blood loss (EBL).
2. Postoperative variables: length of hospital stay (LOS) and analgesic requirements.
3. Surgical complications: In studies reporting sufficient data, the overall complications were subdivided into the following:
 - 3.1 Intraoperative complications: bowel perforation
 - 3.2 Postoperative complications: sexual dysfunction, incisional hernia, urinary dysfunction, and perineal wound infection and pain.
4. Oncological variables: local recurrence (LR) rate, overall survival rate, and positive CRM rate. Any tumor located less than 1 mm from the circumferential margin was defined as positive according to previous evidence [12].

Other additional outcomes reported in some of the articles were also reviewed. LR rates, rates of involved CRM, and rates of intraoperative bowel perforation were evaluated as main outcome measures in a pooled analysis.

Statistical analysis

The present meta-analysis was performed according to the recommendations of the Cochrane Collaboration and the Quality of Reporting of Meta-analyses (QUORUM) guidelines [13, 14]. The weighted mean differences (WMDs) and the relative ratios (RRs) were used to compare continuous and dichotomous variables, respectively. If continuous variables were measured in different units, the standardized mean differences (SMDs) were used. All outcomes were reported with 95 % CIs. The hazard ratio (HR) was used as a summary statistic for long-term outcomes (survival analysis) as described by Parmar et al. [15]. For studies that presented continuous data as medians and ranges, means and SDs were

calculated using the technique described by Hozo et al. [16]. Yates' correction was used for studies that contained a 0 in one cell of a number of events of interest in one of the two groups [17].

Statistical heterogeneity between studies was considered not statistically significant when the Cochrane Q test *P* value was >0.1. The I^2 statistic, the standard heterogeneity test, was used to assess the consistency of the effect sizes. In addition, an I^2 value of less than 25 % was defined to represent low heterogeneity, a value between 25 and 50 % was defined as moderate heterogeneity, and a value of 50 % was defined as high heterogeneity [18]. The fixed-effect (FE) model was first used to pool the results, which assumes that all the studies share the same common (fixed or nonrandom) effect. The random-effects (RE) model was reported if there was heterogeneity between studies. Otherwise, the FE model was reported [19].

The methodological quality of randomized controlled trials (RCTs) was assessed using the Cochrane Risk of Bias Tool [20]. The methodological quality of observational studies was assessed using the nine-star Newcastle–Ottawa Scale [21]. The quality of studies was assessed in accordance with six criteria in three domains: cohort selection, cohort comparability, and outcome. Stars were awarded for each criterion, and a score of 0–9 (allocated as stars) was allocated to each study. Studies achieving a score of 7 stars were considered to be of high quality.

To determine the extent to which the combined risk estimate might be affected by individual studies, sensitivity analysis was performed for RCTs and high-quality retrospective studies with the exclusion of the most heavily weighted studies. Publication bias was evaluated using funnel plots.

Meta-analysis was conducted by Review Manager Version 5.0 (The Cochrane Collaboration, Oxford, London, UK). The statistical tests were two-sided, and *P* values of <0.05 were considered statistically significant.

Results

Description of eligible studies

Eight studies [7–11, 22–24] published from 2008 to 2012 fulfilled the inclusion criteria and were included in the meta-analysis (Fig. 1). The characteristics of included studies are shown in Table 1. A total of 949 patients (ELAPE 496, APE 453) from eight studies were included. One study [8] was an RCT, one study was a prospective case–control study [10], and the remaining studies were retrospective observational. All were single-center studies except that one was a multi-center study [11]; the selected studies were matched in terms of demographic

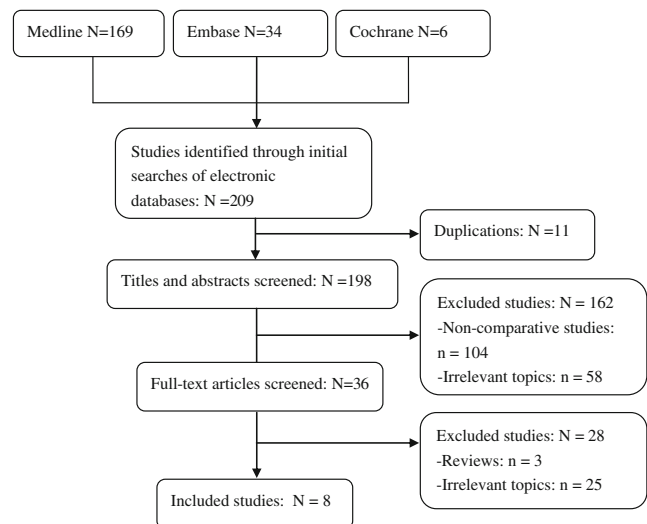


Fig. 1 Flow diagram of studies identified, included, and excluded

data, tumor characteristics, operative data, and postoperative outcomes. The total number of patients per study ranged from 21 to 300. Examination of the reference lists of these studies did not detect any further studies for evaluation.

Methodological quality of included studies

Agreement between the two reviewers for study selection and validity assessment was 95 and 96 %, respectively. Full-length articles were all available for review. The RCT did not provide information regarding the blinding method. Follow-up time ranged from 1 to 130 months. For the retrospective observational studies, the risk of bias was evaluated using the Newcastle–Ottawa Scale (Table 2). Five studies scoring 7 stars were considered to be of high quality. Data were prospectively collected in two studies. Both groups of the six trials [7, 8, 10, 22–24] were from the same institution during the same time period. Exposure ascertainment and postoperative assessment were confirmed by surgical records. All studies were comparable for age, gender, and clinical stage. Seven studies [7–11, 22, 24] were comparable for pre-operative chemoradiotherapy or radiotherapy. Three studies were comparable for body mass index (BMI). The matching was also performed in terms of American Society of Anesthesiology (ASA) score, tumor size, tumor height, and tumor grade.

Meta-analysis of perioperative variables

1. Pooled data from the three studies [7, 8, 10] that reported operating time for rectal cancer showed that no significant difference between ELAPE and APE in operating time

Table 1 Characteristics of included studies

Year	First author	Study design	No. of patients: ELAPE/APE	Clinical stage	Neoadjuvant therapy: ELAPE/APE	Response to neoadjuvant therapy	Adjuvant therapy: ELAPE/APE	Comparability	Mean follow up (median): ELAPE/APE	Study quality (score)
2010	West NP	Retro	176/124	T0–T4	RT ^b 130/90 CT ^c 84/48	NA	None	1, 2, 4, 5, 8	From admission to discharge	★★★★★★★
2012	Vaughan-Shaw PG	Case-control	16/20	T2–T4	RT 7/9 CT 9/7	NA	NA	1, 2, 3, 4, 8, 9	370 days	★★★★★★★
2012	Angenete E	Retro	38/31	NA	RT 28/28 RCT ^d 9/0 ^c	NA	13/10	1, 2, 3, 4, 8, 9	44 months (13–84)	★★★★★★★
2012	Asplund D	Retro	79/79	T0–T4	RT 60/66 RCT 15/5 ^c	NA	NA	1, 2, 4, 5	26(1–88)/45(1–89)months	★★★★★★★
2012	Han JG	RCT ^a	35/32	T3–T4	RCT 10/9	NA	NA	1, 2, 3, 4, 5, 6, 8	29(12–48)/22(14–46)months	RCT
2012	Barker JA	Retro	12/9	T2–T3	RT 7/1 ^c RCT 0/2 ^c	NA	NA	1,2,4,8	1–8 years; median not stated	★★★★★★★
2012	Martijnse IS	Retro	134/112	T3–T4	Yes	NA	NA	1, 2, 4, 8	1–10 years; median not stated	★★★★★★★
2012	Sigmar Stelzner	Retro	28/46	T1–T4	Yes	25/36	NA	1, 2, 4, 5, 7, 8	1–13 years; median not stated	★★★★★★★

Comparability variables: 1 = age, 2 = gender, 3 = BMI, 4 = clinical stage, 5 = tumor height, 6 = tumor size, 7 = tumor grade, 8 = preoperative therapy, 9 = ASA score

NA data not available

^a Randomized controlled trial

^b Radiotherapy

^c Chemotherapy

^d Radiochemotherapy

^e There were significant differences between the groups

Table 2 Risk of bias in the observational studies using Newcastle–Ottawa rules

Year	First author	Representative cohort/reference	Exposure ascertainment	Comparability	Assessment	Follow-up	Possible selection bias	Missing data and other
2010	West NP	Yes/same; patient base	Surgical records	Matched in 1, 2, 4, 5, 8	Independent blind	Details provided	Possible bias in patient selection	None
2012	Vaughan-Shaw PG	Yes/same; prospectively collected data	Surgical records	Matched in 1, 2, 3, 4, 8, 9	Record linkage	Details provided	Minimal, data were prospectively collected	None
2012	Angenete E	Yes/same; patient base	Surgical records	Matched in 1, 2, 3, 4, 9	Record linkage	Details provided	Possible bias in patient lost to follow-up	No data we focused missed
2012	Asplund D	Yes/same; patient base	Surgical records	Matched in 1, 2, 4, 5	Record linkage	Details provided	Possible bias in patient selection	Some data on CRM were missing
2012	Han JG	Yes/same	Surgical records	Matched in 1, 2, 3, 4, 5, 6, 8	Record linkage	Details provided	Minimal, data were prospectively collected	None
2012	Barker JA	Yes/same; patient base	Surgical records	Matched in 1, 2, 4, 8	Record linkage	Details not available	Possible bias in patient selection	None
2012	Martijnse IS	Yes/different; patient base	Surgical records	Matched in 1, 2, 4, 8	Record linkage	Details provided	Possible bias in patient selection	Unclear
2012	Sigmar Stelzner	Yes/same; patient base	Surgical records	Matched in 1, 2, 4, 5, 7, 8	Record linkage	Details provided	Possible bias in patient selection	None

Comparability variables: 1 = age, 2 = gender, 3 = BMI, 4 = clinical stage, 5 = tumor height, 6 = tumor size, 7 = tumor grade 8 = preoperative therapy, 9 = ASA score

(RE: WMD 48.26 min; 95 % CI -36.37 to 132.89; *P* = 0.26).

2. Pooled data from the two studies [7, 8] that reported EBL showed blood loss was slightly less in ELAPE than APE (FE: WMD -100.45 mL; 95 % CI -151.37 to -49.52; *P* = 0.0001).

Meta-analysis of postoperative variables

According to analysis of the four studies [7, 8, 10, 11] that reported LOS, there were no significant differences between ELAPE and APE in LOS (RE: WMD -1.43 days; 95 % CI -3.12 to 0.26; *P* = 0.10). Two studies reported analgesic requirements, but different analgesics were used in different disease phase. One study used opiate for 1–5 days at a median of 2 days [10], and one used nonsteroidal anti-inflammatory drugs and oral tramadol for patients with a positive VAS score [8]. Only one study reported comparative data of analgesic requirements in detail and found no significant difference between ELAPE and APE (*P* = 0.29).

Meta-analysis of surgical complications

There were no significant difference in overall complication rate between ELAPE and APE (FE: RR 0.93; 95 % CI 0.66–1.32; *P* = 0.69). This result remained significant after Bonferroni correction. There were no significant differences between ELAPE and APE in postoperative complication rate, such as perineal wound complication (RE: RR 0.72; 95 % CI 0.33–1.55; *P* = 0.39), urinary dysfunction (FE: RR 1.53; 95 % CI 0.88–2.67; *P* = 0.13), or sexual dysfunction (FE: RR 1.27; 95 % CI 0.85–1.89; *P* = 0.24) (Table 3).

Meta-analysis of oncological variables

The intraoperative bowel perforation rate was significantly lower in ELAPE than in APE (FE: RR 0.34; 95 % CI 0.21–0.54; *P* < 0.00001) (Fig. 2). Pooled data from the eight studies [7–11, 22, 23] that reported positive CRM rates showed ELAPE significantly reduce the rate of CRM involvement compared with APE (FE: RR 0.44; 95 % CI 0.34–0.56; *P* < 0.00001) (Fig. 3).

The local recurrence of ELAPE was significantly lower than that of APE (RE: RR 0.32; 95 % CI 0.14–0.74; *P* = 0.008) (Fig. 4). Three studies [8–10] reported overall, disease-free, and recurrence-free survival rates, and these outcomes were not suitable for meta-analysis. These studies did not show a significant difference between ELAPE and APE. Vaughan-Shaw et al. [10] demonstrated that disease-free survival was 100, 90, and 80 %, respectively, at a median follow-up of

Table 3 Overall analysis of ELAPE vs APE

Outcome of interest	No. of studies	No. of patients, ELAPE/APE	WMD /RR (95 % CI)	P	Study heterogeneity			
					Chi-squared test	df	I ² (%)	P
Perioperative variables								
Operating time, min	3	87/83	48.26 [-36.37, 132.89]	0.26	24.12	2	92	<0.00001
EBL, mL	3	73/63	-100.45 [-151.37, -49.52]	0.00	0.03	1	0	0.86
Postoperative variables								
LOS, days	4	263/207	-1.43 [-3.12, 0.26]	0.10	7.90	3	62	0.05
Surgical complications								
Overall complication	2	47/41	0.93 [0.66, 1.32]	0.69	0.54	1	0	0.46
Postoperative sexual dysfunction	2	40/32	1.27 [0.85, 1.89]	0.24	0.05	1	0	0.83
Postoperative urinary dysfunction	3	62/64	1.53 [0.88, 2.67]	0.13	1.01	2	0	0.60
Postoperative urinary infection	2	48/44	0.35 [0.09, 1.45]	0.15	0.83	1	0	0.36
Perineal wound complication	5	239/162	1.05 [0.71, 1.55]	0.81	10.93	4	63	0.03
Perineal wound infection	4	89/107	0.53 [0.24, 1.17]	0.12	0.50	3	0	0.92
Oncological variables								
Intraoperative bowel perforation	6	301/276	0.34 [0.21, 0.54]	<0.00001	3.44	5	0	0.63
Local recurrence	7	468/407	0.32 [0.24, 0.44]	<0.00001	14.67	6	59	0.02
Positive CRMs	7	511/539	0.44 [0.34, 0.56]	<0.00001	7.06	7	1	0.42

527 days in ELAPE, laparoscopic APE, and open APE. Three-year oncologic outcome of Martijnse's study [9] showed the overall survival improved from 83 to 92 % after the approach of ELAPE was introduced to their institution. Han et al. [8] performed a Kaplan–Meier test in the overall survival and disease-free survival after ELAPE and conventional APE for rectal cancer, and no statistically significant difference was shown. The mean length of the overall survival in the ELAPE group was 45 months and in the conventional APE group 40 months ($P=0.202$, log-rank test).

Sensitivity analysis

The sensitivity analysis (Supporting information Table S1) included one RCT, one case–control study, and four retrospective studies, which scored more than 7 stars on the Newcastle–Ottawa Scale. The results were all consistent with the above outcomes. Heterogeneity between studies was not significantly reduced by the sensitivity analysis in terms of LOS, operating time, and perineal wound complication. Heterogeneity

between studies focused on local recurrence was significantly reduced ($I^2=13\%$, $P=0.33$).

Publication bias

The funnel plots for positive CRM rate and intraoperative bowel perforation rate are shown in Fig. 5. The number of studies included in our analysis, less than eight, indicated potential publication bias. All study outcomes were within the 95 % CIs and were distributed symmetrically, showing the publication bias was minimal.

Discussion

This meta-analysis included eight studies comparing ELAPE with APE. The results showed that ELAPE had a lower recurrence rate, positive CRM rate, and intraoperative bowel perforation rate than APE and that ELAPE had a longer operating time and a shorter LOS than APE. We found no significant differences between the groups in other outcomes.

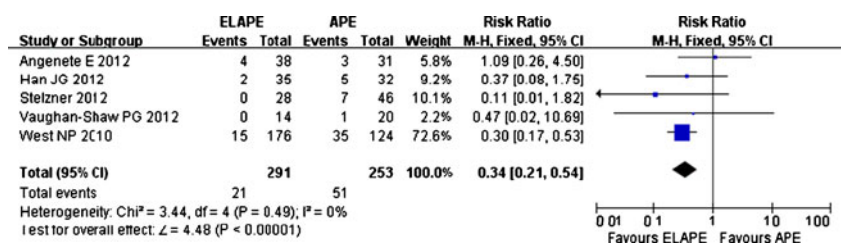
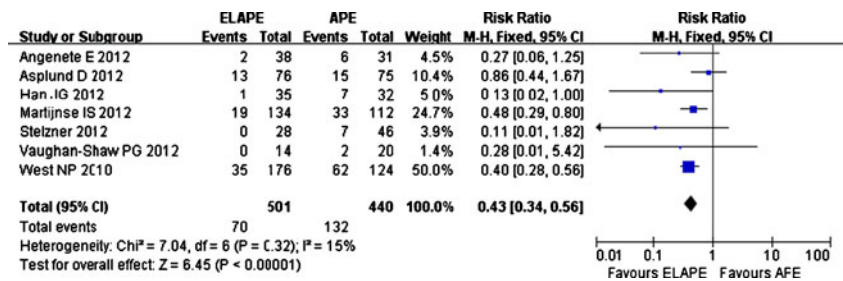
Fig. 2 Meta-analysis of intraoperative bowel perforation

Fig. 3 Meta-analysis of CRM involvement



In our series, ELAPE had a statistically longer operating time than APE; this result was to be expected, because of the challenges of adopting a newer technique. Nevertheless, in keeping with trends observed in other areas of colorectal practice, experience with ELAPE would increase. In addition, ELAPE requires the prone jackknife position, and the coccyx is often removed in continuity with the main specimen to improve direct visualization of the dissection and thus has a simplified perineal part [6], which makes ELAPE faster possible.

We demonstrate a significant reduction of the intraoperative bowel perforation rate and positive CRM rate of ELAPE as compared to conventional APE. Porter et al. [25] could demonstrate that the perineal dissection in APE is the vulnerable phase for perforation, accounting for 62 % of all events. With conventional APE, the resulting specimen frequently has a waist at the lower border of the mesorectum, and the CRM is often close to the rectal muscle tube [4]. ELAPE involves mobilization of the mesorectum as far down as the origins of levator muscles and ischioanal fossa fat attached to the specimen en bloc, a more cylindrical specimen is created. It enables better visualization for the traditionally difficult perineal dissection, thus reducing the chances of entering the wrong surgical plane and perforating the specimen, which should increase the amount of tissue removed around the tumor and, therefore, reduce CRM positivity and intraoperative bowel perforations.

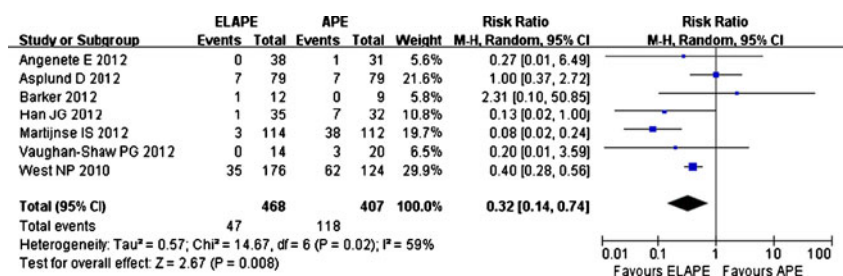
There was no significant difference in overall and postoperative complication rate between these two groups. Unfortunately, studies reported overall complication rate without reporting all the specific events, which may have introduced bias. Urogenital dysfunction was the most popular complication in both the cylindrical and conventional APE groups in our study. There was no significant difference between them. APE is

one of the most common risk factors for postoperative sexual dysfunction, whereas the stage and the size of the tumor do not seem to have an influence [26]. Sexual function has been known to depend on the integrity of the pelvic autonomic nervous plexuses. Sexual dysfunction can be caused by damage at the level of the superior hypogastric plexus or the hypogastric nerves before they join together with the parasympathetic nerves at the inferior hypogastric plexus [27]. The clear identification of pelvic anatomic landmarks might be useful for the successful achievement of both negative CRMs and the preservation of urogenital functions during cylindrical APE.

Only studies reported for perineal flap reconstructions in cylindrical procedure were included in our analysis. No significant difference was found in wound complication rate between groups. Perineal wound complications have been reported to occur in as many as in 10.7–66.7 % of patients [8, 10, 11, 22, 24]. These complications can include wound infection, dehiscence, and herniation in studies included. Obesity, co-morbidity, preoperative irradiation, and intraoperative bleeding were identified as predisposing factors [28]. If the resulting pelvic floor defect is too large for primary closure during the extended dissection of cylindrical APE, a gluteus maximus flap reconstruction or insertion of a prosthetic mesh may be performed [6]. There was a tendency toward a reduction in wound complications in the extralevator group when a muscle flap was used. Various flap techniques may be used to reduce the risk of local wound complications. Bilateral V-Y fasciocutaneous flaps and VRAM flap were reported in studies we reviewed.

The local recurrence rate and positive CRMs rate were significantly lower in ELAPE than in APE. The length of follow-up varied among studies, which could be a potential source of bias. Only three studies reported overall and recurrence-free survival

Fig. 4 Meta-analysis of local recurrence



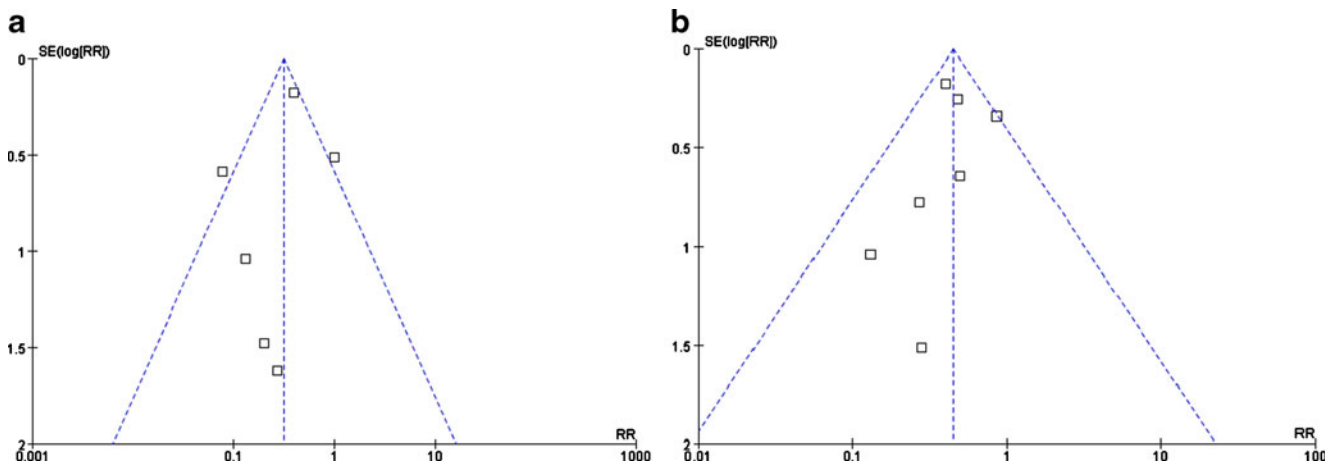


Fig. 5 Funnel plots of **a** positive CRM rate and **b** intraoperative bowel perforation rate

rates of 1–5 years, and these studies did not report follow-up time in detail, which made it impossible to compare long-term survival rates. Long-term follow-up of the patient groups in these studies would be useful. It is well established that CRM involvement and intraoperative perforation appear to be well-documented determinants of the prognosis of low rectal cancer [2, 4, 29, 30]. Septic complications of the perineal wound are associated with a higher rate of local recurrence [31], and no difference is found in perineal wound infection rate between groups. The bond between higher local recurrence rate and higher CRM positivity rate is expected, since irradical resections result in high local recurrence rates.

Compared with meta-analysis of all the studies, the RCT did not show any differences between groups in any of the outcomes studied. Although a meta-analysis of RCTs only would be ideal, there were too few RCTs to enable us to draw any definitive conclusions. We performed a further sensitivity analysis including the RCT and the high-quality retrospective studies. The results remained similar to those of the overall analysis, which confirmed the reliability of the pooled estimates in the meta-analysis.

We concluded that ELAPE is more efficient and equally safe compared with APE in appropriately selected patients. Long-term follow-up in future studies is needed to evaluate the oncological outcomes of the two approaches.

The present meta-analysis has the following limitations that must be taken into account. First, except for one small-scale RCT and one prospective case–control study, all the studies included were observational, and the small number of cases in several studies also decreased the reliability of the results, which made it difficult to acquire strong evidence for the conclusions. Second, the studies included in the analysis were mostly conducted at major institutions, and therefore, the patients evaluated might not reflect patient populations in the community. Third, heterogeneity between studies was low for most of the dichotomous variables examined in this analysis, but was marked for all the continuous variables. There was

significant variability in terms of definitions, inclusion criteria, exclusion criteria, operating technique, and measurement of outcomes. It was not possible to match all patient groups for age, BMI, tumor stage, preoperative therapy, and previous abdominal history. All these factors may have contributed to the high heterogeneity between studies. Use of the RE model for pooled data might minimize the effects of heterogeneity, but does not abolish them. The degree of heterogeneity fell for most outcomes with sensitivity analysis, but this difference was not significant. Fourth, some perioperative data reported as median (range) were calculated to reach the mean (SD) values with the techniques introduced in literature [16], and it is considered a limitation of the data analysis in the current study. Finally, some authors did not report the proportion of patients lost to follow-up, which may influence the reliability of the conclusions.

To our knowledge, this is the first meta-analysis comparing ELAPE and APE for rectal cancer. This study was conducted at an appropriate time because enough data have accumulated for inspection by meta-analytical methods at a time when ELAPE is used more frequently for rectal cancer all over the world. We applied multiple strategies to identify studies, strict criteria to include and evaluate the quality of the studies, and sensitivity analysis to minimize the effects of heterogeneity. Sensitivity analyses confirmed the reliability of the pooled estimates in the meta-analysis, and the pooled results were all consistent with the overall effect. In addition, almost all the baseline characteristics were comparable between the ELAPE and APE groups in each retrospective studies. Thus, selection bias had a limited effect on the final pooled outcomes. This analysis therefore provides the most up-to-date information in this area.

Conclusion

The present meta-analysis suggests that ELAPE has a lower intraoperative bowel perforation rate, positive CRM rate, and

local recurrence rate than APE. In selected low rectal cancer patients, ELAPE is a more efficient and equally safe option to replace APE. Despite our rigorous methodology, the inherent limitations of the included studies should be considered, and conclusions drawn from our pooled results should be interpreted with caution. Future RCTs will be useful to confirm this conclusion.

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Conflict of interest The authors declare that they have no conflict of interest.

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