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REVIEW ARTICLE – COLORECTAL CANCER

Standard Versus Extralevator Abdominoperineal Low Rectal Cancer Excision Outcomes: A Systematic Review and Meta-analysis

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Background. The extended, extralevator abdominoperineal excision has been described with the aim of improving oncological low rectal cancer patient outcomes.
Materials and Methods. A systematic literature review was conducted using Medline/PubMed, Embase, Cochrane library, and Ovid for standard and extralevator abdominoperineal rectal cancer excision studies between 1995 and 2013. A total of 1,270 articles were identified and screened, and of these, 58 reports (1 randomized, 5 case–control and 52 cohort studies) were included for the qualitative analysis, and 6 were included for the quantitative analysis. The primary endpoints included intraoperative tumor perforation, the circumferential resection margin involvement, local recurrence rate, and the perineal wound complication rate. The secondary endpoints included the length of postoperative hospital stay and quality of life. Comprehensive Rev Men, version 5.2 was used for the statistical calculations.
Results. A significant difference in the circumferential resection margin involvement rate [odds ratio (OR) 2.9; $p < .001$], intraoperative perforation (OR 4.30; $p < .001$), local recurrence rate (OR 2.52; $p = .02$), and length of hospital stay (OR 1.06; $p < .001$) in favor of the extended group was observed. Additionally, the perineal wound complications were higher in the extended group (OR 0.62; $p = .007$). No difference in quality of life was observed.
Conclusions. Our analysis confirms the oncological advantages of the extended abdominoperineal excision method. Although the perineal wound complications were higher, the length of postoperative hospital stay was shorter, and quality of life was not inferior to the conventional resection method.

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After the first description of a total mesorectal excision (TME) by Heald in 1982, this technique has spread among surgeons and has become the gold standard for rectal cancer surgery, leading to significant improvements in local recurrence rates and survival.[1,2] Despite the application of TME principles, oncological results appeared to be inferior for abdominoperineal excisions (APE) compared with low anterior resections.[3,4] The former, however, is hampered by a higher local recurrence rate (up to 30 %) in spite of aggressive adjuvant therapy.[4] In fact, performing a TME on the levator plane and excising the anal canal via the perineal approach results in a "waist" specimen at the puborectalis level, with limited tissue surrounding the tumor. This procedure may expose patients to tumor perforation risks, which are estimated to occur in 13.7 and 28.2 % of cases, and circumferential resection margin risks, which are involved in 12–49 % of cases.[5,6] Both of these factors are known local recurrence predictors.[7,8] This unfavorable oncological outcome has prompted a renewed interest in improving the APE surgical technique. Recently, a more radical APE surgical approach has been described, termed the extralevator APE (ELAPE).[9] The goal of this extended approach, which is closer to the original Miles operation, is to achieve an R0 resection while performing a wide "cylindrical" excision without opening the space between the tumor and the levator ani.[10] Although several studies have compared the two techniques, no definitive answer has been achieved whether one approach is superior to the other.

The aim of this systematic review and meta-analysis was to compare the standard (sAPE) and extended APE outcomes with respect to surgical factors and cancer-related parameters.

METHODS

Literature Research Strategy

A systematic literature search was conducted with the terms "abdominoperineal," and "excision," [or] "resection," [and] "rectal neoplasm," and related Medical Subject Headings (MeSH) using the Medline/PubMed, Embase, Cochrane library and Ovid databases. Reference lists of the retrieved articles were checked for further relevant contributions. The retrieved research reports began in 1995 because TME was expected to be implemented in most colorectal units around that time. No language restrictions were applied. A manual search of the references was performed by two independent reviewers, and any decision about inclusion or exclusion was made based on a consensus. Any disagreements were resolved by third-party adjudication.

Through database searching, 1,270 articles were identified and were then screened for excluding reviews, meta-analyses, case reports, abstracts, and letters. When several studies from 1 institution that referred to the same database in the same period were found, the most informative report was chosen to avoid any potential overlap. The inclusion criteria comprised articles addressing low rectal carcinoma patients, studies that provided at least one of our outcome measures, and studies where detailed patient information was provided.

Endpoints

The primary endpoints were: intraoperative tumor perforations (IOP), the circumferential resection margin (CRM) involvement, the local recurrence (LR) rate, and the perineal wound complication (PWC) rate.

The secondary endpoints were: the postoperative hospital length of stay (HS) and quality of life (QoL).

Data extracted from the articles included: first author, year of publication, study design, number of patients who underwent APE or ELAPE, number of patients who received neoadjuvant or adjuvant therapies, number of patients with intraoperative perforation, with postoperative wound complications, with CRM involvement at pathological examination, length of postoperative hospital stay, number of patients with local recurrence, and results of QOL questionnaire. Data extraction was restricted to cases operated on with curative intent

Two of the authors (V.S., G.C.), independently reviewed the studies included in our meta-analysis using the Newcastle-Ottawa scale for nonrandomized clinical trials and the Cochrane Collaboration Tool for assessing the risk of bias for the only randomized clinical trial included.[11] Any disagreement was resolved by consensus. A positive CRM was defined in the majority of the studies as the presence of a tumor within 1 mm of the resection margin. For the evaluation of the LR rates, only studies with a minimum median follow-up period of 24 months were included to reduce biases that might result from an insufficient follow-up period.

PWCs were classified as minor and major. Minor wound complications were defined as any wound complication that did not need a further surgical intervention. The major wound complications included conditions that needed further surgical interventions or long-term management.

A QoL analysis was achieved with the "European Organization for Research and Treatment of Cancer" (EORTC) questionnaire QLQ C30 (an integrated system for assessing the health-related QoL of cancer patients in international clinical trials). The main Global Health Status (GHS), Physical Functioning (PhF), Emotional Functioning (EmF), and Social Functioning (SoF) scores were considered. All scales ranged from 0 to 100. A high functional scale score (PhF, EmF, SoF) represented a high functioning level.

For each endpoint, the patients were divided into two major groups, which included a sAPE and an ELAPE group.

Statistics

The patient demographic details, information regarding the designated primary and secondary endpoints, study characteristics, and the neoadjuvant and/or adjuvant therapy information were collected.

The dichotomous data were pooled for events, and the odds ratios (OR) and 95 % confidence intervals (95 % CI) were calculated.

For the continuous data, the weighted mean differences (WMDs) were calculated using means and standard deviations (SD). The I^2 statistic was used to assess the impact of any heterogeneity on the meta-analysis. When the heterogeneity test was statistically significant, a random effects model was used; otherwise, a fixed effects model was used. According to the guidelines, $I^2 = 0$–40 % was considered to be a lack of heterogeneity, $I^2 = 30$–60 % represented moderate heterogeneity, $I^2 = 50$–90 % represented substantial heterogeneity, and $I^2 = 75$–100 % represented considerable heterogeneity.[11]

The exclusion impact in the individual studies was evaluated using the chi-square test to weigh and adjust for any inhomogeneity in the studies.

Comprehensive Rev Men version 5.2 was used for the statistical calculations.

RESULTS

A total of 58 articles were included in a qualitative synthesis (1 randomized, 5 nonrandomized case control, and 52 cohort studies) and 6 in a quantitative synthesis (a meta-analysis that included 1 randomized and 5 nonrandomized case control studies) (Fig. 1).

Quality of Studies and Risk of Bias

The majority of included studies were small, with sample sizes ranging from 36 to 318, and from 16 to 176 per group.[12–15] Only two of the reported trials were multicenter, and there was only one randomized trial.[14,16,17] All studies were comparable for age, gender, and clinical stage. Preoperative chemoradiotherapy was less common in the standard group in 1 study, as was long-course preoperative radiotherapy in another study.[13,16]

The length of follow-up was reported by three studies and varied between 1 and 89 months.[13–15] Patients lost to follow-up were not mentioned in any study. Also, three studies covered a long length of time and compared operations performed in two different periods.[12,16,17] All five nonrandomized clinical trial scored four or more points upon analysis using the Newcastle-Ottawa scale, even if only the Vaughan-Shaw study received points in the comparability section (Table 1).[15] The randomized clinical trial showed an unclear risk of bias in the randomization and a high risk of bias in blinding section.

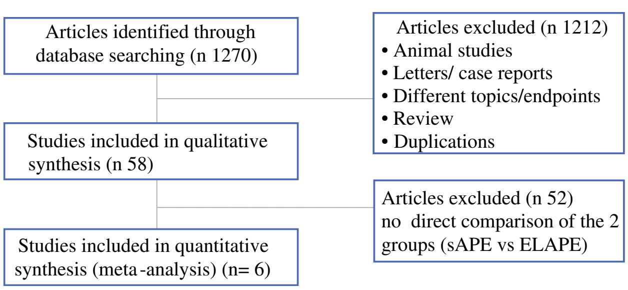


FIG. 1 Flow diagram of studied identified, included and excluded

Intraoperative Perforation and Circumferential Resection Margin Involvement

Data from 26 studies were extracted (1 randomized trial, 5 case–control, and 20 cohort studies) to analyze our primary endpoints. There were 4,304 patients in the sAPE group [2,970 males with a mean age of 65.2 years (range 40–78 years)] and 741 patients in the ELAPE group [444 males with a mean age of 63.9 years (range 45–80 years)]. No significant differences were observed between the groups with respect to age, gender, tumor stage, tobacco use, or the incidence of any comorbid condition (diabetes mellitus, coronary artery disease, congestive heart failure, renal insufficiency, peripheral vascular disease, chronic obstructive pulmonary disease, hematologic, or endocrine disease). The rate of patients undergoing a neoadjuvant radiotherapy (RT) or radio-chemotherapy (RT/CT) was 36.8 % in the sAPE group and 58 % in the ELAPE group.

The IOP and CRM involvement rates in the sAPE group were 11.8 and 17 % versus 5.5 and 12.2 % in the ELAPE group, respectively (Table 2).

The meta-analysis included five observational case–control trials and one randomized clinical trial. A Forrest plot showed a significant difference in the IOP rate, which was in favor of ELAPE (OR 4.30, 95 % CI 2.54–7.29, $p < .001$). Additionally, a fixed effects model was used to validate the overall effect (Fig. 2a). A significant difference in the CRM involvement rate, in favor of ELAPE, was observed (OR 2.90, 95 % CI 1.70–4.96, $p < .001$). A random effects model was used to validate the overall effect (Fig. 2b).

TABLE 1 Characteristics of the studies included in the meta-analysis

Author	Study design			Years of enrolment	Patients APE/ELAPE	Newcastle-Ottawa scale
West[17]	Retrospective	Case–control	Two centers	1997–2007	101/27[a]	****
West[16]	Retrospective	Case–control	Multicenter	1997–2008	124/176[b]	****
Stelzner[12]	Retrospective	Case–control	Monocenter	1997–2010	46/28[c]	****
Asplund[13]	Retrospective	Case–control	Monocenter	2004–2009	79/79[d]	*****
Han[14]	Prospective	Randomized	Monocenter	2008–2010	32/35	[e]
Vaughan Shaw[15]	Prospective	Case–control	Monocenter	2009–2011	20/16	****

* indicates a point on the Newcastle-Ottawa scale

[a] Leeds 99 APE/10 ELAPE (ELAPE from 2005 after training). Stockholm 2 APE/17 ELAPE (from 2001 to 2006)

[b] ELAPE performed by 11 consultants from 9 European colorectal Institutions compared to APE performed by one UK Center

[c] ELAPE from 2006 on, after training of two surgeons

[d] Both procedures performed by nine consultant surgeons

[e] The quality of the randomized study was assessed using the Cochrane collaborations' tool for assessing the risk of bias, and the results are described in the Results section

TABLE 2 Intraoperative perforation, circumferential resection margin involvement, and perineal wound complications in standard and extended APE

sAPE	No. patients	NeoT	IOP	CRM+	PWC
Baker[33]	89	40	9	11	ng
Scheidbach[34]	149	90	16	7	38
Wibe[35]	821	81	131	95	ng
Marr[36]	181	0	48	66	ng
Nagtegaal[3]	373	200	51	108	ng
Tekkis[37]	181	86	12	24	ng
Guillou[20]	76	30	6	17	ng
den Dulk[4]	434	216	64	128	ng
Ptok[38]	956	114	22	42	ng
Strassburg[39]	37	24	6	4	ng
West[17]	101	73	8	15	ng
Chambers[41]	42	25	11	9	9
Kim[42]	50	50	7	11	ng
Anderin[23]	441	313	52	79	ng
West[16]	124	54	35	61	25
Shihab[43]	72	46	10	23	ng
Stelzner[12]	46	46	7	2	19
Asplund[13]	79	71	8	15	22
Han[14]	32	9	5	9	19
Vaughan Shaw[15]	20	16	1	5	7
Total (%)	4,304	1,584 (36.8)	509 (11.8)	731 (17)	130/492 (26.4)
ELAPE	No. patients	NeoT	IOP	CRM+	PWC
Smedh[44]	60	56	10	13	14
Holm[9]	28	28	1	2	4
West[17]	27	19	1	4	ng
Bebenek[45]	210	65	9	16	39
Davies[46]	40	22	1	0	ng
West[16]	176	84	5	35	67
Han[47]	12	3	2	2	1
Stelzner[12]	28	28	0	0	3
Asplund[13]	79	75	10	13	36
Han[14]	35	10	2	2	18
Welsch[48]	30	24	0	2	14
Vaughan Shaw[15]	16	16	0	2	2
Total (%)	741	430 (58)	41 (5.5)	91 (12.2)	198/674 (29.3)

NeoT number of patients undergoing neoadjuvant therapy, *IOP* intraoperative perforation, *CRM+* circumferential resection margin involvement, *PWC* perineal wound complications, *Ng* not given

Local Recurrences

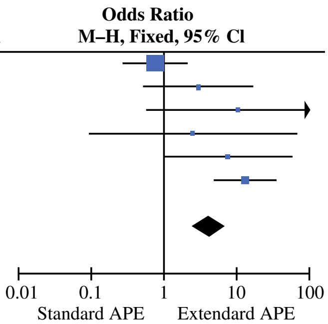
The LR rate was studied by extracting data from 25 articles (including 18 sAPE and 7 ELAPE articles) with a minimum median follow-up period of 24 months. There were 2,911 and 832 patients in the sAPE and ELAPE groups, respectively. The LR rate was 13.1 versus 6.3 % in the sAPE and ELAPE groups, respectively. In the sAPE and ELAPE groups, 37.2 versus 52.8 % of the patients were treated with neoadjuvant therapy, respectively, and 27.1 and 47.2 % were treated with adjuvant therapy, respectively (Table 3).

The meta-analysis showed a difference in the LR rate, which was in favor of ELAPE (OR 2.52, 95 % CI 1.14–5.66, $p = .02$). A fixed effects model was used to yield the overall effect (Fig. 2c).

(a) Intraoperative perforation

Study or Subgroup	Standard APE Events	Standard APE Total	Extended APE Events	Extended APE Total	Weight	Odds Ratio M–H, Fixed, 95% CI
Asplund D, 2012	8	79	10	79	56.8%	0.78 [0.29, 2.09]
Han J, 2012	5	32	2	35	10.2%	3.06 [0.55, 17.01]
Stelzner S, 2011	7	46	0	28	3.3%	10.82 [0.59, 197.28]
Vaughan–Shaw PG, 2012	1	20	0	16	3.2%	2.54 [0.10, 66.59]
West NP, 2008	23	101	1	27	7.7%	7.67 [0.99, 59.60]
West NP, 2010	35	124	5	176	18.8%	13.45 [5.09, 35.53]
Total (95% CI)		**402**		**361**	**100.0%**	**4.30 [2.54, 7.29]**
Total events	79		18			

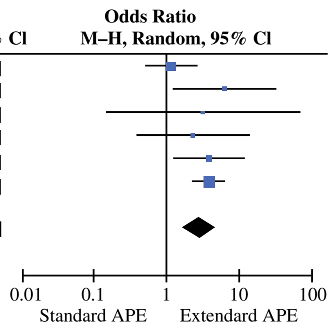
Heterogeneity: Chi² = 17.78, df = 5 (P = 0.003); I² = 72%
Test for overall effect: Z = 5.43 (P < 0.00001)



(b) Circumferential resection margin involvement

Study or Subgroup	Standard APE Events	Standard APE Total	Extended APE Events	Extended APE Total	Weight	Odds Ratio M–H, Random, 95% CI
Asplund D, 2012	15	79	13	79	25.0%	1.19 [0.52, 2.70]
Han J, 2012	9	32	2	35	9.2%	6.46 [1.28, 32.69]
Stelzner S, 2011	2	46	0	28	2.9%	3.20 [0.15, 69.16]
Vaughan–Shaw PG, 2012	5	20	2	16	7.8%	2.33 [0.39, 14.04]
West NP, 2008	41	101	4	27	16.3%	3.93 [1.26, 12.21]
West NP, 2010	61	124	35	176	38.8%	3.90 [2.34, 6.50]
Total (95% CI)		**402**		**361**	**100.0%**	**2.90 [1.70, 4.96]**
Total events	133		56			

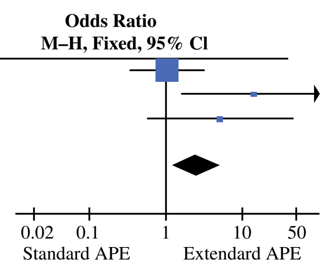
Heterogeneity: Tau² = 0.12, Chi² = 7.07, df = 5 (P = 0.22); I² = 29%
Test for overall effect: Z = 3.90 (P < 0.0001)



(c) Local Recurrence

Study or Subgroup	Standard APE Events	Standard APE Total	Extended APE Events	Extended APE Total	Weight	Odds Ratio M–H, Fixed, 95% CI
Asplund D, 2012	7	79	7	79	78.6%	1.00 [0.33, 3.00]
Han J, 2012	9	32	1	35	8.5%	13.30 [1.58, 112.25]
Stelzner S, 2011	7	46	1	28	13.0%	4.85 [0.56, 41.69]
Total (95% CI)		**157**		**142**	**100.0%**	**2.54 [1.14, 5.66]**
Total events	23		9			

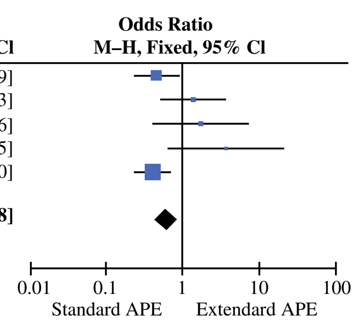
Heterogeneity: Chi² = 5.43, df = 2 (P = 0.07); I² = 63%
Test for overall effect: Z = 2.28 (P = 0.02)



(d) Perineal wound complications

Study or Subgroup	Standard APE Events	Standard APE Total	Extended APE Events	Extended APE Total	Weight	Odds Ratio M–H, Fixed, 95% CI
Asplund D, 2012	22	79	36	79	31.8%	0.46 [0.24, 0.89]
Han J, 2012	19	32	18	35	8.5%	1.38 [0.52, 3.63]
Stelzner S, 2011	8	46	3	28	3.8%	1.75 [0.42, 7.26]
Vaughan–Shaw PG, 2012	7	20	2	16	1.8%	3.77 [0.66, 21.55]
West NP, 2010	25	124	67	176	54.1%	0.41 [0.24, 0.70]
Total (95% CI)		**301**		**334**	**100.0%**	**0.62 [0.44, 0.88]**
Total events	81		126			

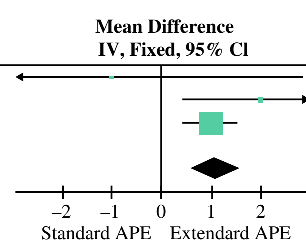
Heterogeneity: Chi² = 11.86, df = 4 (P = 0.02); I² = 66%
Test for overall effect: Z = 2.70 (P = 0.007)



(e) Postoperative hospital length of stay

Study or Subgroup	Standard APE Mean	Standard APE SD	Standard APE Total	Extended APE Mean	Extended APE SD	Extended APE Total	Weight	Mean Difference IV, Fixed, 95% CI
Asplund D, 2012	11	10.25	79	12	13.75	79	1.7%	–1.00 [–4.78, 2.78]
Han J, 2012	11	3.75	32	9	2.75	35	9.9%	2.00 [0.41, 3.59]
West NP, 2010	15	2.5	124	14	2	176	88.4%	1.00 [0.47, 1.53]
Total (95% CI)			**235**			**290**	**100.0%**	**1.06 [0.57, 1.56]**

Heterogeneity: Chi² = 2.54, df = 2 (P = 0.28); I² = 21%
Test for overall effect: Z = 4.18 (P < 0.0001)



◀ **FIG. 2** Forrest Plots of **a** intraoperative perforation, **b** circumferential resection margin involvement, **c** local recurrence, **d** perineal wound complications, and **e** postoperative hospital length of stay

TABLE 3 Local recurrence rate following standard and extended APE

sAPE	No. patients	NeoT	AdjuT	LR
Baker[33]	89	40	49	27
Scheidbach[34]	149	90	76	10
Law[49]	69	10	21	16
Chuwa[50]	38	0	0	2
Chambers[41]	42	25	11	2
Ferenschild[51]	65	36	0	24
Hermanek[52]	143	0	11	27
Kneist[53]	24	1	4	2
Wibe[35]	821	81	54	99
Lee[54]	159	79	76	12
Marr[36]	181	0	22	43
Chiappa[55]	65	18	29	4
Strassburg[39]	14	5	6	1
Kim[42]	50	50	37	10
Anderin[23]	441	313	289	42
Kusters[56]	436	218	0	47
Stelzner[12]	46	46	40	7
Asplund[13]	79	71	64	7
Total (%)	2,911	1,083 (37.2)	789 (27.1)	382 (13.1)
ELAPE	No. patients	NeoT	AdjuT	LR
Nissan[57]	282	123	234	18
Dehni[58]	91	49	29	9
Okaro[59]	76	27	13	6
Smedh[44]	58	56	23	1
Bebenek[45]	157	48	11	7
Davies[46]	40	22	8	2
Silberfein[60]	128	115	75	10
Total (%)	832	440 (52.8)	393 (47.2)	53 (6.3)

NeoT number of patients undergoing neoadjuvant therapy, *AdjuT* number of patients undergoing adjuvant therapy, *LR* local recurrence

Perineal Wound Complications

The PWC data were extracted from 17 articles (7 on sAPE and 10 on ELAPE). The PWC rate was 26.9 % in the sAPE group and 29.3 % in the ELAPE group. Moreover, 63.2 % of the patients received neoadjuvant therapy in the sAPE versus 55.1 % in the ELAPE group (Table 2). There were 14.4 % major and 12.5 % minor PWCs in the sAPE group and 10.1 % major and 19.2 % minor PWCs in the ELAPE group.

The meta-analysis demonstrated a difference in the overall PWC rate that was in favor of sAPE (OR 0.62, 95 % CI 0.44–0.88, $p = .007$). A fixed effects model was used to yield the overall effect (Fig. 2d).

Postoperative Hospital Length of Stay

HS data were extracted from two observational case–control studies and 1 randomized study. A significant difference in the mean HS, which was in favor of the ELAPE group, was observed (OR 1.06, 95 % CI 0.57–1.56, $p < .001$). A fixed effects model was used to yield the overall effect (Fig. 2e).

Quality of Life

For the QoL evaluation, data were extracted from seven cohort studies and one case–control study that reported data from the EORTC QLQ-C30 questionnaires. The Global Health Status reports demonstrated a mean score of 72.5 for the sAPE group versus 75.7 for the ELAPE group (Table 4). Additionally, each main element of the reported functional scales was also comparable (PhF, 78.8 vs 83.4; EmF, 81.9 vs 78.4; SoF, 76.8 vs 76.2).

DISCUSSION

The introduction of the TME as a rectal cancer treatment has been associated with a reduction in local recurrence rates.[4] However, when performing an APE, due to the lack of mesorectal fat in the distal ano-rectum region, the surgical procedure produces a “waist” at the point in which the abdominal component of the operation joins the perineal component. This procedure may result in greater resection margin involvement or perforation risks.[18] The introduction of the extralevator abdominoperineal excision aimed at a wider “cylindrical” ano-rectum excision, thus enabling the removal of the extra tissue encompassing the tumor which provides an adequate tissue barrier, as demonstrated by evaluating the extended compared with the standard APE specimens with tissue morphometry.[16–18]

As advocated by Holm et al., the extended procedure should improve the inadvertent rectal perforation and CRM rates.[9] These two factors were identified as predictors of adverse outcomes, namely, local recurrences and impaired survival.[7]

Our analysis demonstrated that the IOP rate is higher for the sAPE technique. In accordance with the implementation of the neoadjuvant therapies during the last decades, a higher rate of perioperative RT/CT was used for the ELAPE group; however, although the neoadjuvant therapy caused downstaging of the tumor and, coupled with tumor shrinkage, impacted the CRM status, perforation occurrence is solely attributable to the surgical technique.[19]

Our study also demonstrated a significant increase in the CRM involvement rates in the standard operation patient group. This difference was maintained after the case–

TABLE 4 QLQ-C30 scores following standard and extended APE

sAPE	No. patients	GHS	PhF	EmF	SoF
Allal[61]	11	78	87	84	85
Grumann[62]	23	71.7	89	77.9	82.5
Camilleri-Brennan[63]	53	69.5	70.6	83.2	78
Gosselink[64]	51	78	82	87	73
Schmidt[65]	28	71.2	66.1	66.8	75.3
Sideris[40]	42	67	87	83	77
Vaughan Shaw[15]	20	78	77.2	88.2	75
Total (mean score)	228	(72.5)	(78.8)	(81.9)	(76.8)
ELAPE	No. patients	GHS	PhF	EmF	SoF
Welsch[48]	30	70.6	80	70	68
Vaughan Shaw[15]	16	85.4	90	94.3	91.7
Total (mean score)	46	(75.7)	(83.4)	(78.4)	(76.2)

GHS global health status, *PhF* physical functioning, *EmF* emotional functioning, *SoF* social functioning

control and randomized study Forrest plots were conducted.

According to other observations, the reduced CRM and IOP occurrences reflect the lower local recurrence rate in the extended procedure with respect to the standard APE.[20] In our analysis, the local recurrence rate was estimated considering that the neoadjuvant and adjuvant therapy rates used in each major group were a statistically significant element of our endpoints. Our meta-analysis demonstrated that ELAPE is also an independent predictor of lower local recurrence rates. The previous reviews, which included six and eight studies, both concluded that ELAPE was oncologically superior.[21,22] Asplund et al., however, described a group of patients who were operated on by the same surgeons over a short time period; the results did not show any oncological advantage for extralevator excisions, and, on the contrary, they showed an increase in perineal wound complications and healthcare resources, a higher number of wound revisions, and longer operating times and hospital stays.[13]

Recently, the advantages of changes in the operative position from the Lloyd-Davies to the prone jackknife position during the perineal phase of the procedure have been highlighted. The prone position allows for an excellent view of the most critical dissection area along the posterior wall of the prostate or vagina and the structures of the pelvic diaphragm. It has also been demonstrated that the bowel perforation rate is higher when the operation is performed with patients in the Lloyd-Davies position, even in the extralevator APE group.[23] Additionally, according to Tayyab, ELAPEs performed in the prone jackknife position result in a more cylindrical specimen and therefore in lower perforation, CRM involvement, and local recurrence rates.[24] These data are still conflicting, whereby other authors did not find any significant differences between the two positions.[25]

Overall survival in low rectal cancer patients after the introduction of the TME is largely determined by systemic rather than local relapses.[26] The benefit of extended versus standard APE regarding survival was not determined in our review because of the limited number of studies at our disposal for analysis.[14,27]

Despite the better oncological outcomes, a significant increase in PWC (especially infections and abscesses) after ELAPE has been observed as a result of large perineal defect formations.[28] PWCs have been linked to tumor stage, diabetes mellitus, BMI, smoking, and, most importantly, neoadjuvant therapy.[29] In our analysis, these elements were highly comparable. The previous meta-analysis that evaluated PWC included only patients with perineal flap reconstructions and failed to demonstrate any significant difference between the two techniques.[8] On the contrary, in our analysis, all of the different closing techniques were included. Although reconstruction is not always absolutely required for wound closure, excision of the levator muscles leaves only fatty tissue and skin. This primary closure defect results in tension, which leads to a high wound problem frequency, in particular after neoadjuvant therapy.[30] Chan et al. observed no major PWCs in a patient subgroup with primary closures and without preoperative CRTs, which supports the deleterious effects of radiotherapy on wound healing.[31] Considering the present neoadjuvant treatment indications, the role of perineal reconstructions, as a means to reduce this negative outcome, should be better studied.

The higher PWC occurrences did not entail a QoL impairment, as reported by Vaughan Shaw et al.[15] The authors noted a similar incidence in buttock pain despite the removal of the coccyx and a more extensive pelvic dissection. Moreover, improved urinary incontinence and sexual dysfunction QoL scores were identified in the ELAPE group. This leads to the question of whether the extended perineal dissection causes more harm to the autonomic nerve structures and in particular to the pudendal nerve branches and lower pelvic plexus region.[32] The small number of cases analyzed and the nonstandardized interval until questionnaire completion limit the conclusions that can be drawn from these findings; therefore, more studies should be performed to clarify this aspect.

Interestingly, the length of hospital stay, although resulting from a limited number of studies, demonstrated that ELAPE, despite the more extensive pelvic dissections and higher perineal complication rate, provided shorter hospitalization durations than sAPE.

The present study has several limitations. The number of studies included in the meta-analysis is small, and this can designate a publications bias. As a matter of fact, the rate of abdominoperineal excision has progressively decreased in the last decades as a result of conservative sphincter-saving techniques such as intersphincteric or transanal surgery. Moreover, the diffusion among the surgical community of the abdominoperineal extralevator technique is relatively recent, and thus small prospective series have to be expected. Another limit is related to the nature of the studies; the majority of them were small series, retrospective, and nonrandomized studies: 3 of 5 of the retrospective studies compared historical series of sAPE with patients treated by ELAPE, usually performed by a small number of surgeons and after a surgical training program. Another potential bias is represented by the long time period of data collection by some of the studies, including patients operated on between 1997 and 2010, with only two studies comprising data referring to the same period.[12,13,15–17] Different strategies in rectal cancer management, major changes in the postoperative care since the introduction of the "ERAS" pathway, the evolvement of treatment regimens, and the progressive implementation of neoadjuvant therapy for rectal cancer, and the introduction of laparoscopy, in the last two decades, may further contribute to the short- and long-term outcome and should be taken into account in the interpretation of the results.

In conclusion, our analysis confirms the preliminary data as to some oncological advantages of this procedure and supports the notion that the postoperative QoL in these radically treated patients is acceptable and not inferior to conventional APE procedures. Prospective studies are needed to identify factors and conditions that can help to select the patients who are at a higher risk for perineal complications or poorer oncological outcome.

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