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Title: A pilot randomized study comparing extralevator versus conventional abdominoperineal excision for low rectal cancer after neoadjuvant chemoradiation

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Abstract:

Aims: To assess the feasibility of performing extralevator abdominoperineal excision (ELAPE) after neoadjuvant chemoradiation, compare the rates of circumferential resection margin (CRM) involvement, intra-operative perforation (IOP) and amount of tissue removed around the muscularis propria (MP)/internal sphincter (IS) of the lower rectum in patients with low rectal cancer undergoing ELAPE as compared to conventional abdominoperineal excision (CAPE) after NCRT.

Methods: This was an open-label, parallel arm pilot randomized trial conducted in India. Twenty patients were randomised to one of the study arms. The surgical specimens were fixed, serially cross-sectioned and photographed. Using specialised morphometry software, the amount of tissue resected with each operation was measured.

Results: There was a non-significant trend towards more intra-operative perforations (30% vs 0%, $p=0.06$) and a higher CRM involvement rate (40% vs 20%, $p=0.32$) in the CAPE arm. ELAPE removed a significantly greater amount of tissue around the IS/MP when compared to CAPE ($1911.39 \pm 382\text{mm}^2$ vs $1132.03 \pm 371\text{mm}^2$ [SD], $p<0.001$). The mean distance from the IS/MP to the CRM was significantly greater in the ELAPE arm in the posterior ($28.28 \pm 3\text{mm}$ vs $9.63 \pm 3\text{mm}$ [SD], $p<0.001$) and lateral ($13.69 \pm 3\text{mm}$ vs $9.72 \pm 3\text{mm}$ [SD], $p=0.009$) parts of the rectum but not in the anterior part ($6.74 \pm 2\text{mm}$ vs $6.10 \pm 4\text{mm}$ [SD], $p=0.64$). The short-term morbidity was not significantly different between the two procedures.

Conclusion: ELAPE removed more tissue in the lower rectum and resulted in a lower rate of IOP and CRM involvement when compared to CAPE even after NCRT.

Registered with Clinical Trial Registry of India (CTRI no:2013/05/003661)

Keywords: abdominoperineal excision, extralevator abdominoperineal excision, circumferential resection margin, intra-operative perforation, morbidity

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What does this paper add to the literature: This paper shows that extralevator abdominoperineal excision removes more tissue around the internal sphincter/muscularis propria of the lower rectum than a conventional abdominoperineal excision and thus has the potential to reduce the chances of circumferential margin involvement and intra-operative perforations even after neoadjuvant chemoradiation.

Introduction:

Abdominoperineal excision (APE) is a commonly performed operation for low rectal cancer in many parts of the world in spite of the advancements in neoadjuvant treatments and sphincter preserving techniques [1,2]. However, APE is associated with a higher local recurrence rate and poorer survival when compared to low anterior resection for higher tumours [3,4,5]. This adverse outcome has been attributed to the plane of surgery during conventional APE as practiced nowadays which follows the principle of total mesorectal excision and cones down on the rectal tube at the level of the pelvic floor in contrast to the original procedure described by Ernest Miles. This leads to an increased incidence of involved circumferential resection margin (CRM) and intra-operative perforation (IOP) [6,7]. Therefore, an alternative technique called cylindrical APE or extralevator abdominoperineal excision (ELAPE) was proposed [8] which is more similar to the Miles procedure. Earlier studies have shown that ELAPE removes more tissue outside the muscularis propria (MP)/ internal sphincter (IS) of the lower rectum resulting in a reduced incidence of involved CRM and IOP when compared to a conventional APE (CAPE)[9,10,11]. However, these were either non-randomized studies or included many patients who did not receive neoadjuvant chemoradiation (NCRT). Locally advanced low rectal cancers, especially those needing an APE are considered high risk for recurrence and hence neoadjuvant chemoradiation (NCRT) is recommended for these tumours [12]. NCRT is known to cause tumour downstaging and a subsequent reduction in the rates of involved CRM [13,14,15]. Although logically the group of patients receiving NCRT are those with locally advanced tumors and hence would benefit more with a procedure like ELAPE, it is still unclear whether the tumour downstaging effect of NCRT will negate the advantages of an ELAPE. The primary objective of this study, therefore, was to assess the feasibility of performing ELAPE after NCRT and to compare the short-term outcomes of ELAPE and CAPE in patients who have received NCRT.

Materials and Methods:***Study design and Patients:***

This was a pilot open-label randomized, parallel arm study conducted between May 2013 and December 2015. The primary objective was to study the feasibility of performing ELAPE after NCRT and to compare the rates of CRM involvement, IOP, specimen gradings and amount of tissue removed around the rectum in patients with low rectal cancer undergoing ELAPE as compared to conventional APE. The secondary objective was to compare the intra-operative complications, blood loss, operative time and perineal wound complications between the two groups. Since there is a wide variation in the rates of CRM involvement and IOP following ELAPE and conventional/standard APE in previous studies, most of which were retrospective and in different time periods, we felt the need for a pilot study and hence sample size calculation was not attempted. A total of 20 patients were enrolled and randomized into one of the treatment arms. Patients between 18-70 years of age with a histologically confirmed adenocarcinoma of the lower third rectum (within 5cm from anal verge), clinically staged as T3 and/or N1-2 using MRI, and deemed to require an APE with a curative intent following neoadjuvant chemoradiation were eligible to participate in this study. Patients with tumours involving the prostate or posterior vaginal wall that could be resected en-bloc with a sleeve of the prostate or posterior vagina were also included. However, patients with a locally advanced disease invading the pelvic walls and distant metastasis unresectable for cure were excluded. Other

exclusion criteria were ECOG performance status ≥ 3 , poor cardiopulmonary function, pregnancy, uncontrolled psychiatric disorders and any other contra-indication to general anaesthesia.

While the surgeries were performed in Chennai, India, the tissue morphometric analysis was performed in Leeds, UK. The study was approved by the institutional ethical committee and registered with Clinical Trial Registry of India (CTRI no:2013/05/003661). All patients provided written informed consent.

Randomisation and masking:

Eligible patients were randomly assigned to conventional (CAPE) or extralevator (ELAPE) abdominoperineal excision in a 1:1 ratio using a random number table generated by a computer program for the proposed sample size. Randomisation was stratified according to gender. The random allocation sequence was generated at the Department of Epidemiology and Tumor Registry at our institution and the randomisation code was conveyed to the principal investigator over telephone. The patients and surgeons were not masked. However, the investigator performing the morphometric analysis was masked to the type of surgery.

Procedures:

Neoadjuvant chemoradiation consisted of 50.4Gy external radiation to the pelvis delivered at a rate of 180cGy/day for 28 days along with oral capecitabine (daily dose of 825 mg/m²). Patients were reassessed after 4-6 weeks by clinical examination and MRI scans. Surgery was performed 6-8 weeks after completion of chemoradiation. All the surgeries were performed by a single surgeon.

In the CAPE arm, the surgery was performed in the conventional way where during the perineal phase, the levator muscle was cut close to the rectum on either side from below upwards removing only a cuff of the muscle. The perineal defect was closed primarily in two layers.

In the ELAPE arm, the perineal phase of the surgery was performed in the prone position as described by Holm et al [8], following the plane outside the levator to its insertion and removing the muscle completely. The perineal defect was closed using a unilateral gluteus maximus musculocutaneous flap in the initial five cases and a fascioadipose flap in the subsequent ones.

Photographs of the intact fresh specimen were then taken using a digital camera in the anterior, posterior and lateral aspects with a metric scale to allow calibration (Fig.1). Close-up views were taken in addition of the levators and any suspected defects or perforations. The specimen was then processed according to standard histopathological techniques by fixing in formalin for at least 48 hours and then serially cross-sectioning at 5m intervals from the distal margin to the anterior peritoneal reflection [16]. The slices were labelled from proximal to distal and photographed together and individually with a metric scale and label.

The specimens were graded according to the quality of the mesorectum (mesorectal, intramesorectal or intramuscular plane) and the quality of the levators/sphincters (levator, sphincteric or intrasphincteric plane) according to the UK LOREC guidelines [6]. Extralevator surgery was defined as the presence of additional levator ani muscle in the region of the lower rectum and anal canal with an intact external sphincter. This was confirmed by one of the authors (NPW) from

the specimen photographs, who was blinded to the trial arms. Conventional APE was confirmed from the specimen photograph by the presence of a 'waist' and absence of levator ani muscle.

Primary end-points: CRM status and IOP were assessed on routine histopathological examination. Tumor regression was graded according to the Dworak system [17]. Using specialized morphometry software (Aperio ImageScope, Vista, CA), the amount of tissue resected with each operation was determined. Specific measurements were taken in the distal 10 slices including the area outside of the muscularis propria/internal sphincter (MP/IS) and linear distances to the anterior, posterior and lateral CRMs as already described previously [3,10]. Post-operative complications were graded according to the Clavien-Dindo scoring system [18] at the time of discharge. All demographic, intra-operative, post-operative, pathological and morphometric data were entered into a prospective database. Although the study ended at the time of discharge, the patients continue to be followed up as per the usual institutional protocol.

Statistical analysis:

Statistical analysis was performed using SPSS for Windows (version 17.0; SPSS Inc, Chicago, IL). Student t-test for equality of means under independent samples setting was employed to ascertain the statistical significance. Chi-square test for independence was used to test for the differences in proportions of variables measured in categorical scale. Mann Whitney U test was employed to test the statistical significance of variables measured in ordinal scale between the two groups. A p value <0.05 was considered statistically significant.

Results:

Patient demographics:

The details of the patients and the treatment are given in Table 1. Abdominoperineal excision was performed in 53 patients during the period of the trial of which 20 eligible patients who gave informed consent were randomized- 10 patients into the CAPE arm and 10 into the ELAPE arm. All the twenty patients completed treatment in the arm they were assigned to (Fig.2). The mean age of patients in the CAPE arm was lower than that of the ELAPE arm. The mean tumor size was significantly different higher in the CAPE arm compared to ELAPE (3.15 ± 0.52 vs 2.5 ± 0.66 , $p=0.03$). Although the median duration of surgery was significantly longer in the ELAPE arm, there was a non-significant trend towards lesser blood loss in the ELAPE arm when compared to the CAPE arm.

Specimen grading and pathological details:

In the ELAPE arm, the plane of dissection at the level of the sphincters was in the levator plane in all patients but 3 patients had a defect into the sphincters. However, in the CAPE arm, 50% of patients had surgery in the sphincter plane and 50% in the intrasphincteric plane. Total mesorectal excision was performed in the mesorectal plane in all patients in the ELAPE arm whereas in the CAPE arm, one patient had a dissection in the intramesorectal plane.

The post-operative pathological staging data are given in Table 2. The mean tumour size was significantly larger in the CAPE arm. However, there was no significant difference in the post-treatment T stage, N stage or number of positive lymph nodes between the two arms. Four patients in the ELAPE arm had a complete pathological response when compared to none in the CAPE arm.

The CAPE arm had a higher rate of involved CRM (40% vs 20%, $p=0.32$). While in the ELAPE arm the involved CRM was in the anterior rectal wall in one patient and lateral wall in another, in the CAPE arm the positive CRM was in the anterior and lateral walls in three patients and in the lateral wall in one patient. There were no IOPs in the ELAPE arm compared to 30% in the CAPE arm ($p=0.06$). All the perforations in the CAPE arm were in the anterior rectal wall. While 50% of CRM positive resections had an IOP, only 16.6% of CRM negative resections had an IOP, and conversely, an involved CRM was seen in 66.6% and 28.5% of patients with or without an IOP respectively.

Tissue morphometry:

The ELAPE procedure removed 69% more tissue outside the IS/MP in the distal ten slices of the resected specimen when compared to CAPE. The mean cross-sectional area of tissue removed outside the IS/MP in the distal ten slices overall was $1911.39 \text{ mm}^2 \pm 382$ (standard deviation [SD]) in the ELAPE arm compared to $1132.03 \text{ mm}^2 \pm 371$ [SD] in the CAPE arm ($p<0.001$). Similarly, the mean area of tissue removed outside the IS/MP per slice was also significantly higher after an ELAPE (Fig.3). We identified a significantly higher mean distance from the IS/MP to the posterior and lateral margins of resection in the ELAPE arm, but not to the anterior resection margin (Fig.4). The overall mean distance from the IS/MP to the CRM was significantly greater in the ELAPE arm (8.4mm vs 16.2mm, $p<0.0001$).

Morbidity:

Clavien-Dindo Grade 3 complications were observed in 50% and 40% of patients undergoing ELAPE and CAPE respectively. These were all perineal wound related complications like wound dehiscence or infection requiring frequent dressings and/or debridement and secondary suturing. None of the patients in the ELAPE arm had loss of the perineal flap. Grade 1 and 2 complications seen included superficial wound infections (abdominal or perineal) that needed to be opened at the bedside or higher antibiotics. The median hospital stay was 13 days (range 11-32) and 17.5 days (range 14-44) in the CAPE and ELAPE arms respectively ($p=0.08$). There was no post-operative mortality in either arm. After a median follow-up of 30 months (range 15-44 months), there were no instances of perineal hernia in the ELAPE arm.

Discussion:

This study has demonstrated the feasibility of performing ELAPE after NCRT. We have shown that ELAPE in a prone position removes approximately 69% more tissue outside of the IS/MP region at the level of the lower rectum and anal canal than CAPE, thus enabling wider margins of resection, which is in line with earlier studies which reported that ELAPE removed 68%-77% more tissue in this region [9-11]. Tissue morphometry was first used by West et al to demonstrate that ELAPE removes a significantly larger amount of tissue in the distal rectum and in slices containing tumour when compared with standard operation using historical controls [9]. They reported that the extralevator procedure removed approximately 14.5 mm of extra tissue at the posterior aspect and 4mm at both the anterior and lateral aspects of the specimen, thereby leading to a lower rate of CRM involvement (14.8% v 40.6%; $p=0.013$). Subsequently, few other studies have also used morphometric analysis to compare ELAPE and CAPE (Table 3). A multicentre non-randomized study [10] that compared ELAPE specimens from 11 surgeons across Europe with standard APE specimens from a single centre in the UK also showed that the median distance from the tumour to the nearest

CRM was significantly greater in the ELAPE group (4.0 versus 1.5 mm; $p < 0.001$) leading to a significant reduction in the CRM involvement (49.6% vs 20.3%, $p < 0.001$). The only randomized trial published so far comparing ELAPE and conventional APE showed that the median CRM distance was longer in the patients undergoing ELAPE (2.2 versus 1.85mm, $p = 0.002$) resulting in fewer patients with positive CRM in the ELAPE group (5.7% versus 28.1%, $p = 0.013$) [11]. We were however unable to demonstrate a significant reduction in the CRM positivity rates after an ELAPE although there was a strong trend towards it. The lack of statistical significance is likely due to the small sample size. While two meta-analyses have shown that the CRM involvement is significantly reduced after an ELAPE [20,21], two others have shown no significant difference [22,23]. As these studies have failed to undertake specimen photography with independent histopathological evaluation, it is not possible to determine the quality of either the extralevator or conventional operation.

We found that CRM involvement was more frequent in the lateral wall when compared to the anterior wall in the CAPE group (four of four vs three of four positive CRMs) whereas it was equally distributed in the anterior and lateral walls in the ELAPE group. However, in the European multicentre study, the most common site of CRM involvement was the anterior wall in both ELAPE and conventional APE [10]. We hypothesise that this difference could be due to the fact that in our study, the ELAPE specimens had a significantly higher mean distance from the IS/MP to the posterior and lateral CRM when compared to CAPE, but not to the anterior CRM. Interestingly, we found that even a non-significant increase in the IS/MP to anterior CRM distance in the ELAPE arm was associated with a less frequent anterior CRM involvement when compared to CAPE (10% vs 30% of positive CRMs). A similar finding was observed in another non-randomized comparative study by How et al, who reported a lesser frequency of anterior CRM involvement in patients undergoing ELAPE in spite of a non-significant difference in the muscularis propria to margin distance in the anterior quadrants when compared to those undergoing CAPE [19].

Intra-operative perforation is recognized as an important prognostic factor in rectal cancer [6]. None of the ELAPE specimens in the present study had an IOP compared to 30% in the CAPE specimens. Three meta-analyses have shown that IOP rates are significantly reduced after an ELAPE [20,22,24] whereas another meta-analysis showed a borderline decrease in the IOP rate after ELAPE [23]. The randomized trial by Han et al did not show a significant reduction in the IOP [11]. A large study from the Swedish colorectal cancer registry showed that although in the entire study group, the IOP rates were not significantly different between ELAPE and CAPE, there were significantly lower rates of perforations after ELAPE for tumours below 4 cm (28% vs 9%, $p = 0.04$) [25]. The median distance of the lower border of the tumour from the anal verge was < 2 cm in both the arms of the current study. The anterior location of the IOP in the CAPE group as well as the absence of IOP in the ELAPE group could be a result of the better visualisation of the anterior dissection plane in the prone position. This is supported by the European multicentre study which showed that even in patients undergoing ELAPE, the IOP rates were significantly lower in those patients where the perineal dissection was done in the prone jack-knife position when compared to the lithotomy position (6.4% vs 20.6%, $p = 0.02$) [10]. This clearly demonstrates that ELAPE in the prone position provides an advantage during the anterior perineal phase of the dissection even for surgeons who are experienced in the conventional procedure. Our observations regarding the association of IOP with the CRM is similar to that of West et al who reported that CRM involvement was significantly higher in specimens which had an IOP when compared to those without (70.8% vs 26.9%, $p < 0.0001$) [9].

The rates of CRM and IOP are likely to be high in patients with advanced low rectal cancer, such as those in this series and even in other series from experienced colorectal surgeons (Table 3). Neoadjuvant chemoradiation can induce tumour downstaging and is therefore advocated in patients where the mesorectal fascia is threatened on the MRI. Rullier et al [14] reported that in cT3 rectal cancer patients who received NCRT, the mean CRM distance was significantly higher when the tumours were downstaged (10mm vs 6mm, $p=0.02$), suggesting that NCRT can reduce the rates of CRM involvement. The role of ELAPE in patients undergoing NCRT is not well defined. The proportion of patients receiving NCRT in published studies comparing ELAPE and APE using morphometric analysis ranged from 0% to 59% [9-11]. In the European multicentre study, among patients who received preoperative long-course chemoradiation therapy, extralevator surgery resulted in a lower rate of CRM involvement (12% vs 49%; $p < 0.001$) and IOP (6% vs 33%; $p < 0.001$) than conventional APE surgery (unpublished data). The present randomised study also suggests that ELAPE can result in a reduction in the frequency of CRM involvement even after NCRT.

We observed a higher incidence of perineal wound morbidity in the ELAPE arm. Although some earlier reports mention that delayed perineal wound healing is significantly higher after ELAPE than after an APE [21,25,26], a few others report comparable perineal wound morbidity [20,22,23]. The uniform use of NCRT in our study would have further contributed to the delayed healing of the perineal wound. A recent nationwide study from Denmark reported that both the extralevator technique and NCRT were independent prognostic factors for long-term perineal wound complications [27]. The technique for perineal closure in the ELAPE arm was changed from a musculocutaneous flap to a fascio-adipose flap during the course of the trial since we felt that this would lead to less functional problems and earlier mobilisation. We did not find any difference in the perineal morbidity between the two techniques although the latter was easier and required less time.

This study is not without its limitations. First, the small sample size makes interpretation of the results difficult. Second, the mean size of the tumours was significantly higher in the CAPE arm. Third, even though there were no significant differences in the clinical or pathological T and N stages between the two arms, the down-staging following NCRT was more profound in the ELAPE arm with a few complete pathological responders. Both these factors could have confounded the CRM involvement rates making interpretation of the results difficult. However, it is unlikely that the small difference in tumor size noticed in this study could have any clinical significance. Finally, since all surgeries were performed by a single surgeon, it could be argued that it lacks generalizability. However, we consider this to be proof of principle that a surgeon who changes his approach from CAPE to ELAPE could improve the oncological outcomes of the surgery with respect to CRM involvement and IOP. This is supported by the findings of the multicentre study, in which the CRM involvement reduced from 39% to 8% and the IOP from 19% to 0% among surgeons who switched from the conventional APE to ELAPE [10].

It is debatable if ELAPE has an advantage in patients who receive NCRT. Even though NCRT has an established and vital role in reducing CRM involvement, ELAPE has also been shown to have an independent effect in this regard [10]. In the European study, the CRM involvement rate was not different in the conventional APE group whether or not NCRT was given. However, in the ELAPE group, NCRT was associated with more negative CRMs (unpublished data). While NCRT can sterilise tumor margins, ELAPE removes more tissue around the tumor resulting in a greater distance to the

CRM. Thus, the two may have an additive effect in reducing CRM involvement. More importantly, the use of NCRT may not have influenced the rates of IOP in this study which is related more to the plane of surgery. Only a larger phase 3 randomised trial could answer the question of the value of ELAPE over CAPE in patients receiving NCRT. Assuming ELAPE reduces CRM involvement from 40% to 20% and based on a 90% power to detect a significant difference ($p < 0.05$, two sided), we estimate that nearly 220 patients would be required to be randomised between the two arms.

Conclusion:

We have demonstrated in this pilot study that ELAPE removes more tissue around the IS/MP of the lower rectum and anal canal than CAPE, which, along with an improved visualisation of the anterior dissection plane during the prone perineal dissection during ELAPE may translate into a lesser incidence of CRM involvement and IOP than CAPE. Only an adequately powered randomised study can throw more light on the additional benefit of performing an ELAPE in patients who receive NCRT.

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Table 1: Clinical and treatment details

Variable	CAPE group	ELAPE group	p value
Mean age (yrs)	45.6± 11.9*	55.8± 11.7*	0.053
Male:Female	7:3	7:3	1.0
Mean distance from the anal verge (cm)	1.3±0.82*	1.4±1.07*	0.87
Mean body mass index (kg/m ²)	21.7± 3.4*	23± 3.3*	0.54
No. of Circumferential tumours	4 (40%)	5 (50%)	0.65
Mean duration (minutes)	201.5± 34.3*	294± 32.6*	<0.001
Mean blood loss (ml)	340± 41.2*	205± 98.4*	0.61
Morbidity (Clavien-Dindo score)			0.47
I & II	6 (60%)	5 (50%)	
III	4 (40%)	5 (50%)	
Median hospital stay (days)	13 (11-32) [†]	17.5 (14-44)	0.08

*Standard deviation, †range

CAPE- conventional abdominoperineal excision, ELAPE- extralevator abdominoperineal excision

Table 2: Pathological outcomes

Variable	CAPE group	ELAPE group	p value
Mean tumour size (cm)	3.15± 0.52	2.5± 0.66	0.03
ypT stage [†]			0.12
ypT0	0	4	
ypT1	0	1	
ypT2	3	2	
ypT3	6	3	
ypT4	1	0	
ypN stage [†]			0.17
ypN0	4	8	
ypN1	4	1	
ypN2	2	1	
Median no. of positive nodes (range)	1 (0-20)	0 (0-5)	0.08
No. of Intra-operative perforation	3 (30%)	0 (0%)	0.06
No. of patients with involved CRM	4 (40%)	2 (20%)	0.32
Mean measurement from the tumour to the distal margin (cm)	3.6± 0.65*	3.8± 1.02*	0.90
Dworak Tumour regression grade			0.15
TRG1	1	1	
TRG2	6	3	
TRG3	3	2	
TRG4	0	4	

*standard deviation, [†]UICC TNM 7th edition, CAPE- conventional abdominoperineal excision ELAPE- extralevator abdominoperineal excision, CRM- circumferential resection margin, TRG- tumor regression grade

Table 3: Comparative studies of tissue morphometry

Author	No. of pts. ELAPE/CAPE	Involved CRM ELAPE/CAPE	Intraoperative perforation ELAPE/CAPE	Median cross-sectional tissue area outside IS /MP (mm ²) ELAPE/CAPE
West NP ⁹ , 2008	27/101	15%/41%*	4%/23%*	2500/1500*
West NP ¹⁰ , 2010	176/124	20%/49%*	8%/28%*	2120/1259*
Han GJ ¹¹ , 2014 [†]	35/32	5.7%/28%*	5.7%/15.6%	2146/1211*
How P ¹⁹ , 2014	10/10	0%/40%	NA	7.7mm/5.6mm [#]
Present study [†]	10/10	20%/40%	0%/30%	1911/1132* [‡]

CRM- circumferential resection margin, IS/MP- internal sphincter/muscularis propria, ELAPE- extralevator abdominoperineal excision, CAPE- conventional abdominoperineal excision

*p<0.05, [#]overall mean distance from IS/MP to CRM, [†]randomized controlled trial, [‡]mean values

Legends for figures:

Fig.1- Photographs of a fresh unopened extralevator abdominoperineal excision specimen: a- anterior view, b-posterior view, c- left lateral view, d- right lateral view

Fig.2- Trial profile

Fig.3- Mean cross sectional tissue area outside the internal sphincter/muscularis propria in the distal 10 slices of the specimen according to type of surgery- extralevator (ELAPE) and standard (CAPE) abdominoperineal excision

Fig.4- Tissue morphometric measurements for extralevator (ELAPE) and conventional (CAPE) abdominoperineal excision: mean distance from the IS/MP to the anterior, posterior and lateral circumferential resection margin over the distal ten slices. *p<0.01 versus CAPE