

Dear Editors and Reviewers:

On behalf of my co-authors, we thank you very much for giving us an opportunity to revise our manuscript, we appreciate editors and reviews very much for their positive and constructive comments and suggestions on our manuscript entitled "*Extralavator abdominoperineal excision for low advanced rectal cancer, where to go*" (ID: 53704). Those comments are all valuable and very helpful for revising and improving our paper. We have studied comments carefully and have made correction which we hope meet with approval. Revised portion are marked in red in the paper. The main corrections in the paper and the responds to the reviewer's comments are as flowing:

Responds to the reviewer's comments:

Reviewer #1:

Response to comment: needs some language polishing.

Response: As Reviewer suggested that we carefully polished the manuscript again with assistance from International Science Editing (<http://www.internationalscience-editing.com>).

Reviewer #2:

Response to comment: Abstract must be re-written because there are some points that are repeated; In the abstract you have to delete "systematic review".

Response: It is really true as Reviewer suggested that parts of the abstract are repeated, and we are very sorry for our negligence of it. We have carefully re-written this part according to the Reviewer's suggestion. A rewritten abstract and core tips as follows:

Abstract

Since its introduction, extralevator abdominoperineal excision (ELAPE) in the prone position has gained significant attention and recognition as an important surgical procedure for the treatment of low advanced rectal cancer. Most studies suggest that because of adequate resection and precise anatomy, ELAPE could reduce the rate of positive circumferential resection margins, intraoperative perforation, and may further reduce local recurrence rate and improve survival. While some studies suggest that extensive resection of pelvic floor tissue may increase the incidence of wound

complications and urogenital dysfunction. Laparoscopic-/ robotic-ELAPE and trans-perineal minimally invasive approach allow patients to be operated in the lithotomy position, and has advantages of excellent operative view, precise dissection and reducing post-operative complications. Pelvic floor reconstruction with biological mesh could significantly reduce the incidence of wound complications and the duration of hospital stays. The proposal of individual-ELAPE could further reduce the occurrence of post-operative urogenital dysfunction and chronic perianal pain. The ELAPE procedure emphasizes precise anatomy and conforms to the principle of radical resection of tumors, which is a milestone operation for the treatment of low advanced rectal cancer.

Core tips: Since extralevator abdominoperineal excision procedure (ELAPE) was proposed, its surgical approach and technique are gradually developing, and recognized by an increasing number of colorectal surgeons. This is a first review to report in detail the research progress and controversies of ELAPE in the last decade including advantages of procedure, incidences on post-operative complications, controversies about operative position, development of laparoscopic/ robotic technologies and proposal of individual treatment/ trans-perineal approach.

Response to comment: Reference # 4 must be not Ca Cancer J Clin, should be the original: LANCET II:1812-1813. 1908.

Response: We have corrected the reference and as follows:
Miles WE. A method of performing abdomino-perineal excision for carcinoma of the rectum and of the terminal portion of the pelvic colon. *Lancet* 1908; 23: 1812-1813.

Response to comment: A graphic comparing different types of APE would help A table with data on each section would help the readers.

Response: Thank you very much for your comments, and we made a table to compare post-operative outcomes between ELAPE and APE, which was showed by table 1. In addition, we used our figures to further introduce the individualized ELAPE technique and trans-perineal minimally invasive approach for ELAPE (see figure 1 and 2).

Reviewer #3:

Response to comment: Words misspelled.

Response: We are very sorry for our misspelling of some words, and we revisited the manuscript and corrected the misspelled words

Response to comment: There is no mention of the concept of studying physical function after ELAPE, and the ongoing RCT comparing gluteus maximus flap with biological mesh.

Response: Considering the Reviewer's suggestion, we have mentioned the content of comparing gluteus maximus flap with biological mesh in our manuscript. In addition, we have discussed the post-operative physical function, such as Sexual function, urinary function and perineal pain, in our manuscript. Thank you very much for your comments.

We tried our best to improve the manuscript and made some changes in the manuscript. We added the content about individual treatment and exploration of transperineal operation. These changes will not influence the content and framework of the paper. And here we did not list the changes but marked in red in revised paper. We appreciate for Editors/Reviewers' warm work earnestly, and hope that the correction will meet with approval.

Once again, thank you very much for your comments and suggestions.

Best Regards.

Yours Sincerely,

Jia-Gang Han

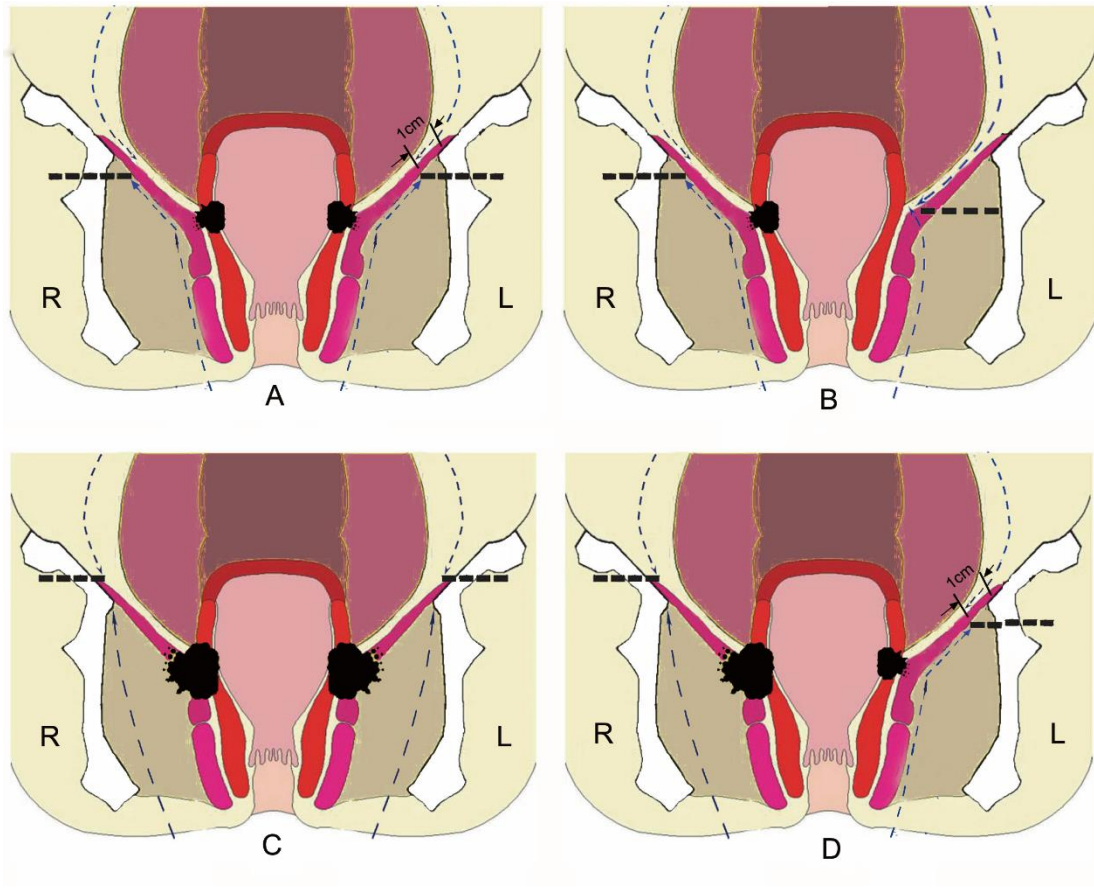


Figure 1 Individualized ELAPE technique^[13, 60].

Note: (A) Tumor not involves the ischioanal fat or levator ani muscle (T3), leave 1 cm of the levator ani muscles on the pelvic sidewall; (B) Tumor locates at one side (T3), levator ani muscle on the other side may be left; (C) Tumor penetrates into the levator ani muscle (T4) bilaterally, dissection should include the fat of the ischioanal fossa and the intact levator ani muscle bilaterally; (D) Tumor penetrates into the levator ani muscle (T4) unilaterally, part of the ischioanal fat and intact levator ani muscle should be dissected unilaterally.

ELAPE, extralevator abdominoperineal excision.

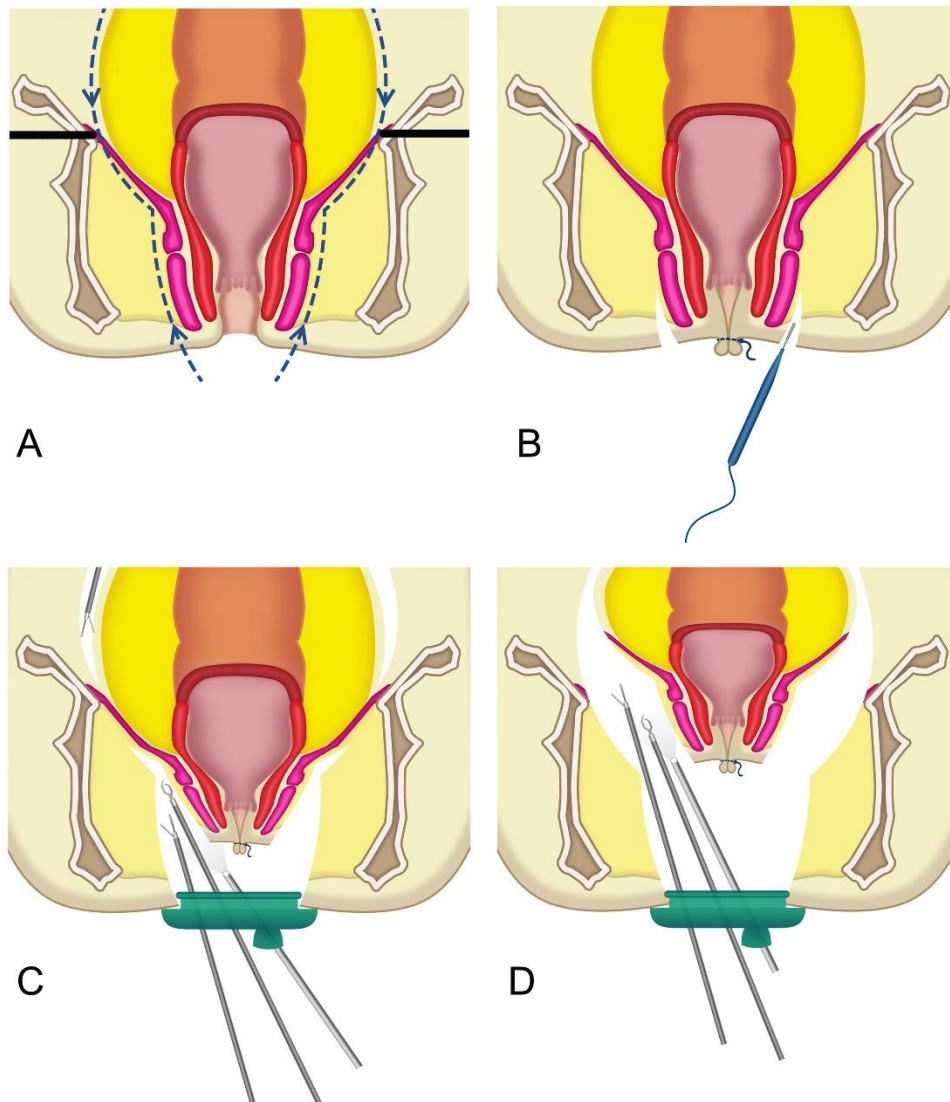


Figure 2 Trans-perineal minimally invasive approach for ELAPE [63].

Note: (A) The resection line of TP-ELAPE; (B) The anus was closed with a purse-string suture and an incision was made around the anus; (C) The dissection was continued outside the external anal sphincter and levator muscle by using the trans-perineal TAMIS platform. The abdominal procedure was performed at the same time; (D) The levator muscles were divided at the lateral most aspect by using the trans-perineal TAMIS platform.

TP-ELAPE, transperineal extralevator abdominoperineal excision; TAMIS, trans-anal minimally invasive surgery.

Table 1 Post-operative outcomes of ELAPE versus APR

Study			Group	n	CRM+ (%)	IOP (%)	Local recurrence (%)	Post-operative complications				QoL scores
Authors	Year	Type						Perineal wound complications (%)	Urinary retention (%)	Sexual dysfunction (%)	Chronic perineal pain (%)	
West NP et al ^[11]	2010	Retro case-control 1	ELAPE/ APR	176/ 124	20.3/ 49.6 <i>P</i> < 0.001	8.2/ 28.3 <i>P</i> < 0.001	-	38/ 20 <i>P</i> = 0.019	46/ 17 <i>P</i> = 0.579	46/ 33 <i>P</i> = 0.192	-	-
Han JG et al ^[13]	2012	RCT	ELAPE/ APR	35/ 32	5.7/ 28.1 <i>P</i> = 0.246	5.7/ 15.6 <i>P</i> = 0.246	2.8/ 18.8 <i>P</i> = 0.048	37.1/ 31.3 <i>P</i> = 0.612	40/ 28.1 <i>P</i> = 0.307	74/ 60 <i>P</i> = 0.306	51.4/ 6.3 <i>P</i> < 0.001	-
Asplund D et al ^[17]	2012	Retro case-control 1	ELAPE/ APR	79/ 79	17/ 20 <i>P</i> = 0.647	13/ 10 <i>P</i> > 0.05	9/ 9 <i>P</i> = 1	46/ 28 <i>P</i> < 0.05	-	-	-	-
Vaughan-Shaw PG et al ^[58]	2012	Pro case-control 1	ELAPE/ LAPR/ OAPR	16/ 10/ 10	0/ 1/ 2 <i>P</i> > 0.05	0/ 0/ 1 <i>P</i> > 0.05	-	2/ 5/ 2 <i>P</i> = 0.21	3/ 2/ 2 <i>P</i> = 0.99	-	-	85.4/ 77.5/ 78.5 <i>P</i> > 0.05
Ortiz H et al ^[66]	2014	Retro case-control 1	ELAPE/ APR	457/ 457	13.6/ 13.1 <i>P</i> > 0.846	7.7/ 7.9 <i>P</i> > 0.902	5.6/ 2.7 <i>P</i> > 0.664	21.9/ 26 <i>P</i> > 0.141	-	-	-	-
Shen Z et al ^[55]	2015	Pro case-control 1	ELAPE/ APR	36/ 33	4/ 12 <i>P</i> = 0.297	5.6/ 21.2 <i>P</i> = 0.028	0/ 15.2 <i>P</i> < 0.034	8.3/ 27.3 <i>P</i> = 0.039	11.1/ 3 <i>P</i> = 0.359	11.8/ 36.4 <i>P</i> = 0.127	-	<i>P</i> > 0.05
Wang XL et al ^[57]	2015	Retro case-control 1	ELAPE/ APR	23/ 25	4.3/ 28 <i>P</i> = 0.028	0/ 20 <i>P</i> = 0.023	8.7/ 32 <i>P</i> = 0.047	39.1/ 24 <i>P</i> = 0.259	26.1/ 12 <i>P</i> = 0.212	60/ 37.5 <i>P</i> = 0.210	47.8/ 8 <i>P</i> = 0.002	<i>P</i> > 0.05
Klein M et al ^[19]	2015	Retro case-control 1	ELAPE/ APR	301/ 253	16/ 7 <i>P</i> = 0.001	2/ 3 <i>P</i> = 0.373	-	14/ 10 <i>P</i> = 0.143	-	-	-	-
Prytz M et al ^[67]	2016	Pro case-control 1	ELAPE/ APR	518/ 209	41.5/ 38.4 <i>P</i> < 0.0001	<i>P</i> < 0.001	<i>P</i> < 0.001	<i>P</i> < 0.001	-	-	-	-
Stelzner S et al ^[16]	2016	Pro case-control 1	ELAPE/ APR	36/ 36	2.9/ 2.8 <i>P</i> = 1	0/ 16.7 <i>P</i> = 0.025	5.9/ 18.2 <i>P</i> = 0.153	16.7/ 36.1 <i>P</i> = 0.061	-	-	-	-

Kamali D et al ^[54]	2017	Pro case-control I	ELAPE/ APR	27/ 21	7.4/ 9.5 <i>P</i> = 0.50	-	3.7/ 4.7 <i>P</i> = 1	37/ 24 <i>P</i> > 0.05	-	-	-	77.3/ 65.3 <i>P</i> = 0.27
Habr-Gama A et al ^[12]	2017	Retro case-control I	ELAPE/ APR	22/ 50	13.6/ 16.6 <i>P</i> = 0.70	0/ 8 <i>P</i> = 0.30	4.5/ 28.6 <i>P</i> = 0.01	22.7/ 46 <i>P</i> = 0.007	-	-	-	-
Carpelan A et al ^[18]	2018	Retro case-control I	ELAPE/ APR	42/ 27	24/ 41 <i>P</i> = 0.136	10/ 22 <i>P</i> = 0.134	7/ 19 <i>P</i> = 0.247	45/ 30 <i>P</i> = 195	-	-	5/ 4 <i>P</i> > 0.05	-
Shen Z et al ^[15]	2019	Retro case-control I	ELAPE/ APR	106/ 88	4.2/ 6.5 <i>P</i> > 0.05	-	3.8/ 11.25 <i>P</i> = 0.027	17.0/ 14.8 <i>P</i> = 0.699	7.5/ 3.4 <i>P</i> = 0.353	-	-	-

ELAPE: extralevator abdominoperineal excision; APR: abdominoperineal excision; RCT: Randomised Controlled Trial; CRM+: positive circumferential resection margins; IOP: intraoperative perforation; QoL: quality of life; LAPR: laparoscopic abdominoperineal excision; OAPR: open abdominoperineal excision.