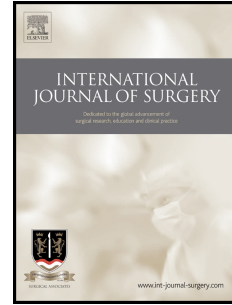


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technique: a systematic review

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**ANTERIOR PERINEAL PLANE FOR ULTRA-LOW ANTERIOR
RESECTION OF THE RECTUM (APPEAR) TECHNIQUE: A SYSTEMATIC
REVIEW**

Running title: APPEAR technique: a systematic review

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1. Introduction

It is recognised that sphincter preservation should be a surgical priority in the management of low rectal cancer [1]. In many cases, the conventional approach to low anterior resection may have several technical disadvantages, which can make accomplishing a low anastomosis very challenging. These include poor visualisation and inadequate control of the distal segment at both resection and anastomosis.

Several novel techniques have been developed in recent years to facilitate preservation of sphincters and restoration of GI continuity. These include intersphincteric resection (ISR), the Anterior Perineal PlanE for Ultra-low Anterior Resection of the Rectum (APPEAR) technique and transanal approaches including transanal minimally invasive surgery (TAMIS) and transanal total mesorectal excision (TaTME). These alternative procedures are not without limitations; they may be technically challenging, unsuitable for locally advanced cases or, in the case of ISR, may inherently lead to inability to satisfactorily preserve the sphincters. As a result, despite this range of new techniques, 20-30% of patients undergoing surgery for rectal cancer are still left with a permanent stoma [2].

The use of the anterior perineal plane to resect the distal rectum was initially described by Cuneo in 1908 and published in a French surgical textbook in 1926 [3] as quoted in a French paper from 1988 [4]. The French surgeons went on to utilise the procedure themselves, publishing a large case series [4]. It is unclear why there was no further uptake of the procedure following this. Use of the anterior perineal approach to perform a rectal anastomosis has been reported intermittently since then [5]. The anterior perineal plane has also been used by colorectal surgeons as one approach to rectocele repair [6] and has been utilised by paediatric surgeons [7,8] and urologists [9,10].

The APPEAR technique was formally described in 2008 [11] and has subsequently been taught and disseminated internationally. The approach utilises a crescentic incision in the anterior perineum to facilitate access to the most distal part of the rectum within the pelvic floor musculature, which is not accessible via the abdomen. This part of the rectum, termed the “rectal no-man’s land”, lies between the superior border of levator ani and the anorectal junction, varying in length from 4-13cm [12]. The APPEAR technique has also been useful, therefore, for proctectomy in patients with inflammatory bowel disease who have dysplasia and to avoid so-called ‘cuffitis’ of the remaining rectum. In addition it may be indicated for reversal of Hartmann’s procedure when this proves difficult via an abdominal approach and also in the rare cases of rectal stricture [5].

The aim of this study was to review use of the APPEAR technique, including all procedures utilising the anterior perineal plane for rectal resection, assessing patient selection, indications, complications and outcomes, both oncological and functional.

2. Material and methods

2.1 Search methods

A literature search was carried out using MEDLINE via PubMed, Embase, Web of Science and Cochrane databases using search terms: anterior; perineal/perineum and rectal/rectum to search within all fields. The databases were searched from inception until the final search date 31/07/2014; no limits were placed on language. The search was conducted with reference to rectal resection, excluding paediatric surgery for anorectal problems but without reference to rectal cancer, to include surgery for other indications.

Following identification of a single publication from a Chinese institution found on PubMed, which made reference to other studies, the search was extended to include the World Health Organization’s Global Health Library and the China Knowledge Resource Integrated Database.

2.2 Selection criteria

Articles were selected following review of title and abstract. The 'related citations' function in PubMed was used to identify further papers; reference lists of selected papers were also searched for any papers missed by the search strategy.

Retrospective and prospective studies were included. Non-randomised studies including case series and case reports were included. Some individual units were noted to have published their results more than once; all papers were included with only data from the most recent publication included in the overall results.

2.3 Data analysis

All papers in Chinese were translated into English. Assessment of papers was carried out by two independent assessors using the Methodological Index for Non-Randomized Studies (MINORS) score [13] to determine the risk of bias in individual studies. Quality scores were included in the results but all papers were included in the analysis as the overall number of studies was low.

Results were reported with means and medians given. It was not appropriate to carry out meta-analysis due to the heterogeneous nature of the studies included and variability in their reporting of outcomes.

3. Results

3.1 Study characteristics

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [14] flow diagram is shown in Fig. 1. The literature search identified thirteen studies from eleven centres in seven different countries. Papers included covered eight case series [4,15-21], four case reports [5,22-24] and one report from a prospective clinical study [11]. Two centres had published results for the same patients twice (at different time points); the earlier study was not included in the totals calculated. With these duplicates removed the overall number included was 174 patients, 102 male and 72 female.

3.2 Patient characteristics and operative details

Table 1 shows the studies identified for inclusion in the review. The quality assessment of studies ranged from a MINORS score of 4 to 10. The case reports showed lower quality scores than the case series. The main areas where the quality of papers was low were: failure to assess consecutive patients or give clear selection criteria; inadequate follow up; unblinded assessment of outcomes and, particularly for the case reports, not assessing all outcomes. Full publications were available for all but one paper [15], for which only the abstract was available and it was therefore not possible to assess quality.

Most papers described the surgical techniques and operative method as per the description of the APPEAR procedure by Williams et al [11]. There were some minor variations; the French surgeons used two teams operating simultaneously, advising that this reduced the duration of surgery although operative time was not reported [4]. In one centre a sagittal incision in the anterior perineum was used in contrast to the usual transverse crescentic incision [16]. All 7 patients were female and also underwent division of the perineal body and posterior vaginectomy with subsequent vaginal repair [16].

The majority of patients (92%) had the abdominal component of their surgery carried out with an open technique, with only 14 patients undergoing laparoscopic resection. Of those for whom operative details were reported, the majority had a stapled anastomosis with an end-to-end configuration. For 1 patient an end-to side anastomosis was created and some anastomoses involved either creation of a colo-pouch or were carried out as part of an ileo-anal pouch procedure. Almost all surgeons carried out defunctioning ileostomy or transverse colostomy on all patients; Le Treut et al. only defunctioned

80% of patients but advised in their discussion that this should be carried out as a 'wise precaution' [4].

Studies varied in their reporting of tumour height from the anal verge. Two of eleven studies did not report this variable (53 patients) [11,18]. One paper gave the average distance from the distal edge of the tumour to the dentate line as 1.3cm with a range of 0.9 to 2.1cm (12 patients) [17]. The remaining seven papers showed the average distance from tumour to the anal verge to be 6.9cm with a wide range from 2 to 13cm.

3.3 Indications for surgery

Table 2 shows the indications for surgery. The majority of cases were carried out for rectal cancer (141 patients, 81%), with a small number for dysplasia (5%) and 6% for other cancers, mainly gynaecological (combined procedures). The remaining 14 patients (8%) underwent surgery, via an anterior perineal approach for benign conditions, including ulcerative colitis and iatrogenic stricture.

Eight out of eleven papers described the staging of rectal cancer using the American Joint Committee on Cancer classification [25]. Two papers used Dukes' classification [26]. Overall 34 patients were TNM stage I, 62 were TNM stage II and 37 were stage III; 1 patient had a complete pathological response. 7 patients underwent surgery for Dukes' D stage rectal cancer, 5 with hepatic metastases and 2 with distant nodal involvement; these were all included in a French publication from 1988 [4]. The majority of patients undergoing surgery for rectal cancer had no details provided about neo-adjuvant therapy, for those that did 45% (18/40) underwent combined chemo-radiotherapy.

3.4 Outcomes

Table 3 shows details of complications. The most frequent complication was fistulation, which was reported by 7 centres. Of the 26 fistulas (24 perineal and 2 vaginal), 6 underwent reoperation; 15 healed with conservative management and 5 required a permanent stoma. The total number of patients who experienced any complication (given that some had more than one) was 51, giving an overall morbidity rate of 29.3%.

Overall 30-day mortality was 2.3% (4 patients); there were 2 further deaths from systemic recurrence, occurring at 3 years and 5 years post-operatively (both had clear margins on histology) [17]. Of the 141 patients who underwent surgery for rectal cancer, no details were given about recurrence for 45 patients, of the remaining patients, 5 developed recurrent cancer, 2 local and 3 systemic. Details of the surgical resection margins were provided for 96 patients and, of these, all had clear margins.

The reporting of functional outcomes was highly variable. Three case reports, gave no information about functional outcomes [5,22,24]. Five studies provided a descriptive account, with incontinence ranging from 0 – 4% [4,16,17,19,21]. One of these also provided results using the Kelly Score, with an average score of 5/6 [16] representing 'good' continence [27]. Two studies gave an average stool frequency of 3/24 hours with a range of 2-7 [18] and 1-8 [11]. Two centres provided greater details, with average Wexner scores of 5.5 in one study [20] and 5 for cancer patients, 2 for patients with ulcerative colitis (UC) in another study [11] out of a maximum score of 20 [28]. These centres also gave details of intact internal anal sphincters [11], anorectal reflexes [19] and unaltered resting and squeeze pressures [11].

Quality of life scores were assessed by two centres, one study used the QLQ-30 rating to assess this, showing an increase in scores over the year following surgery [17]; the other study utilised the SF-36 score and showed no difference in quality of life following surgery, compared with pre-operative scores [11].

The permanent stoma rate was 8/155 (5%). 13 patients (from 3 centres) were still awaiting closure at the time their results were published, 12 of these had a follow up time of less than 12 months; length of follow up was not stated for the remaining patient. Reasons for permanent stoma formation included fistulation, colonic necrosis and stricture.

The follow up period within the studies varied greatly from 2 months to 5 years; five studies had follow up periods greater than 2 years [4,11,16-18].

4. Discussion

The priorities in the surgical management of rectal cancer are to achieve oncological clearance whilst balancing this with optimising bowel function and long-term quality of life. The views of the patient must be an important consideration during the decision making process and some would prefer to accept a less than perfect functional outcome in order to achieve their goal of sphincter-preservation.

The broad range of indications for which rectal surgery via an anterior perineal approach has been carried out, demonstrates the ongoing evolution in surgical techniques. The initial publication from the French surgeons included some patients, with tumours of the upper rectum, and with Dukes' D rectal cancer, who by the current standards of care would not necessarily be considered candidates for an APPEAR procedure [4].

Average tumour height from the anal verge was 6.9cm. This result is skewed by the data from the French study since, with exclusion of these cases, average tumour height would be 4.7cm. The variation in tumour height is likely to represent the learning curve of surgeons carrying out the procedure.

There is also variation between the different centres in the proportion of patients undergoing surgery for benign conditions. The study published from the UK shows a wider range of indications for the APPEAR procedure, particularly for UC and benign stricture. This is likely to reflect the case mix at this unit including tertiary referrals for patients wishing to avoid a permanent stoma [11].

The range of complications arising following APPEAR procedures is similar to that for other rectal resections [29-31]. The overall rate of morbidity (29.3%) is slightly higher than that of 25.8% shown by a recent review of studies of ISR [30] but lower than the Dutch TME trial, which reported an overall morbidity of 45% [31].

In this review, 15% of patients developed a fistula following their surgery; fistulation is a recognised problem following perineal surgery. Measures taken to reduce occurrence included, an extended period of drainage [11,20] and routine examination under anaesthetic at 8-12 weeks to allow repair of any anastomotic defect [11]. Post-operative fistulation also affects patients undergoing ISR; although the recent review of this procedure found a lower overall rate [30], individual studies found rates as high as 19% [32]. It is likely that fistulation partly results from insufficiency of blood supply affecting wound and anastomotic healing. Unfortunately, insufficient details were given in the studies to attempt any analysis to determine risk factors.

The 30-day mortality in this review at 2.3% is in keeping with figures from a meta-analysis of post-operative complications following rectal cancer surgery in 36,315 patients, which showed operative mortality to be 2% [33]. National audit data for England and Wales for 2013 showed 90-day mortality to be 2.5% following elective major resection for rectal cancer [34].

The short duration of follow up in many of the studies makes it impossible, at this stage, to comment on longer-term oncological outcomes of 5-year recurrence and disease-free survival. The high rate of R0 resection (in those reported) is, at least in part, likely to reflect careful case selection. One potential benefit of the anterior perineal approach is the ability to ensure complete excision of the mesorectum by improving access; unfortunately, only one case report provided details of the mesorectal plane of excision achieved [24].

The comparison of functional outcomes between centres and with other surgical techniques is limited by variability in the methods of reporting post-operative bowel function. The mean number of bowel movements in 24 hours and Wexner scores were comparable to those undergoing ISR [29].

The overall permanent stoma rate from these studies was 5%; this did vary considerably between individual centres from 0-31% [11,18]. This compares with a risk of permanent stoma formation following anterior resection varying from 6-23% in single centre retrospective studies [35,36] to 19% in a multicentre randomised trial [37]. Furthermore, success rates of anterior resection for low rectal tumours vary, and in many hands, APER with a permanent stoma continues to be the safe surgical option.

The most recently developed technique to facilitate sphincter preservation is transanal TME. TaTME evolved from a combination of technologies including transanal endoscopic microsurgery (TEM), endoscopic mucosal resection (EMR) and single incision laparoscopic surgery (SILS) [38]. This approach to resection can be used with a transanal approach only or combined with an abdominal approach [39]. With the development of specifically designed equipment, early problems with port dislodgement, maintenance of pneumorectum and achieving adequate exposure are gradually being resolved. The largest published series so far, including 140 patients, shows results equivalent to those for standard TME in terms of operative time, complete resection and macroscopic quality of the TME specimen as well as morbidity and mortality [38]. Long-term oncological results following this procedure are not yet available.

Proponents of perineal and transanal approaches believe that these techniques will be widely adopted, advancing the practice of rectal cancer surgery [40]. Critics feel that the studies have been done on patients with early favourable tumours, that many complications are unreported, and that case selection bias is an issue. There is undoubtedly a steep learning curve, during which care must be taken to avoid complications [41]. It is likely that the rectal cancer surgeon needs to be aware of all these available approaches and techniques which could be used in difficult cases to help minimise the poor outcomes associated with an involved CRM.

The main limitation of this review is that it is primarily based on small retrospective case series and reports. This clearly restricts the interpretation of results but is often the case while a procedure is still in the development stage. None of the studies reported a control group or a denominator so it is unclear how many patients were considered unsuitable for this procedure. This inherent selection bias reflects the experimental nature of the technique. In this review, some complications, for example anastomotic leak, are almost certainly under-reported. Many of the studies included have short follow up periods, limiting ability to compare longer-term oncological and functional outcomes between centres or with other techniques. Low scores for quality assessment reflected these risks of bias for some of the included studies. It was also not possible to conduct meta-analysis due to the heterogeneity of data. However, the review did include all years of publication and papers in any language.

Ideally, a randomised controlled trial would be used to allow direct prospective comparison between the alternative sphincter preserving techniques but this would be very difficult to carry out due to low numbers, lack of equipoise and the difficulty negotiating with an individual patient's beliefs and preferences about stoma formation and acceptable functional outcomes.

5. Conclusions

Use of the anterior perineal plane for rectal resection is likely to remain a selective technique, useful where other procedures may not be suitable, to avoid a permanent colostomy for specific patients, both in benign and cancer cases. It is well suited for use as a combined procedure with laparoscopic resection.

This systematic review has shown comparable morbidity, mortality and short-term oncological outcomes between the APPEAR procedure and other techniques for low rectal resection. Use of this approach has facilitated avoidance of a permanent stoma for a selected group of patients with limited options. Longer-term oncological and functional results are needed to fully determine the role of this procedure.

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Table 1 Included studies with patient characteristics and operative details

Lead author	Country	Year	MINORS score 0-16	Patients (Male: Female)	Median age (range)	Lap	Anastomosis	Hand-sewn	Tumour height from anal verge in cm (range)	Temporary stoma	Pre-operative stoma
<i>Bricot [15]*</i>	<i>France</i>	<i>1985</i>	-	29	-	0/29	-	-	-	-	-
Le Treut [4]	France	1988	6	60 (30:30)	57 (27-82)	0/60	End-to-end	27/60	8.8 (4-13)	48/60	Not stated
Abou-Zeid [5]	Egypt	2007	4	1 (0:1)	Not stated	0/1	End-to-side	0/1	n/a	1/1	1/1
Williams [11]	UK	2008	10	14 (12:2)	54 (21-71)	0/14	5 IAPP (UC) 5 colo-pouch 4 end-to-end	Not stated	Not stated	14/14	3/14 - 1 UC - 3 trauma
Agrawal [16]	India	2008	6	7 (0:7)	42 (37-62)	0/7	End-to-end	7/7	5.5 (5-6)	7/7	0/7
Xiong [17]	China	2011	8	12 (8:4)	56 (51-60)	0/12	Not stated	0/12	1.3 (from dentate)	12/12	0/12
<i>Qiu [23] *</i>	<i>China</i>	<i>2011</i>	<i>4</i>	<i>1 (1:0)</i>	<i>55</i>	<i>1/1</i>	<i>End-to-end</i>	<i>0/1</i>	<i>5</i>	<i>1/1</i>	<i>0/1</i>
Qiu [20]	China	2012	6	26 (19:7)	63 (54-73)	7/26	End-to-end	NS	4.6 (3.9-5.3)	26/26	0/26
Marquardt [24]	German	2012	5	1 (1:0)	69	1/1	End-to-end	0/1	5.5	1/1	0/1
Li [18]	China	2012	6	39 (23:16)	58 (33-79)	0/39	End-to-end	NS	Not stated	Not stated	0/39
Tong [22]	China	2012	5	1 (0:1)	46	1/1	End-to-end	0/1	4	1/1	0/1
Wang [19]	China	2013	4	8 (6:2)	56 (46-67)	0/8	End-to-end	0/8	5 (4-6)	Not stated	0/8
Di Palo [21]	Italy	2013	4	5 (3:2)	72 (60-78)	5/5	Not stated	0/5	3.2 (2-5)	5/5	0/5
Totals/ Averages	Seven	1985 to 2013	Range 4- 10	174 (102:72)	57.6 range 21-82	14 (8.0 %)	146 end-end 1 end-to-side 5 IAPP 5 colo-pouch 17 not stated	34/95 (35.8%) 79 not stated	6.9 cm range 2-13	115/127 (90.6%) 47 not stated	4/114 (3.5%) 60 not stated

Studies in italics and marked with * have results which are duplicated and the patients are not included in the numbers for analysis. *Lap* cases with abdominal component carried out laparoscopically, *NS* not stated, *IAPP* ileo-anal pouch procedure, *UC* Ulcerative colitis, *n/a* not applicable.

Table 2 Indications for surgery and further details of cases carried out for rectal cancer

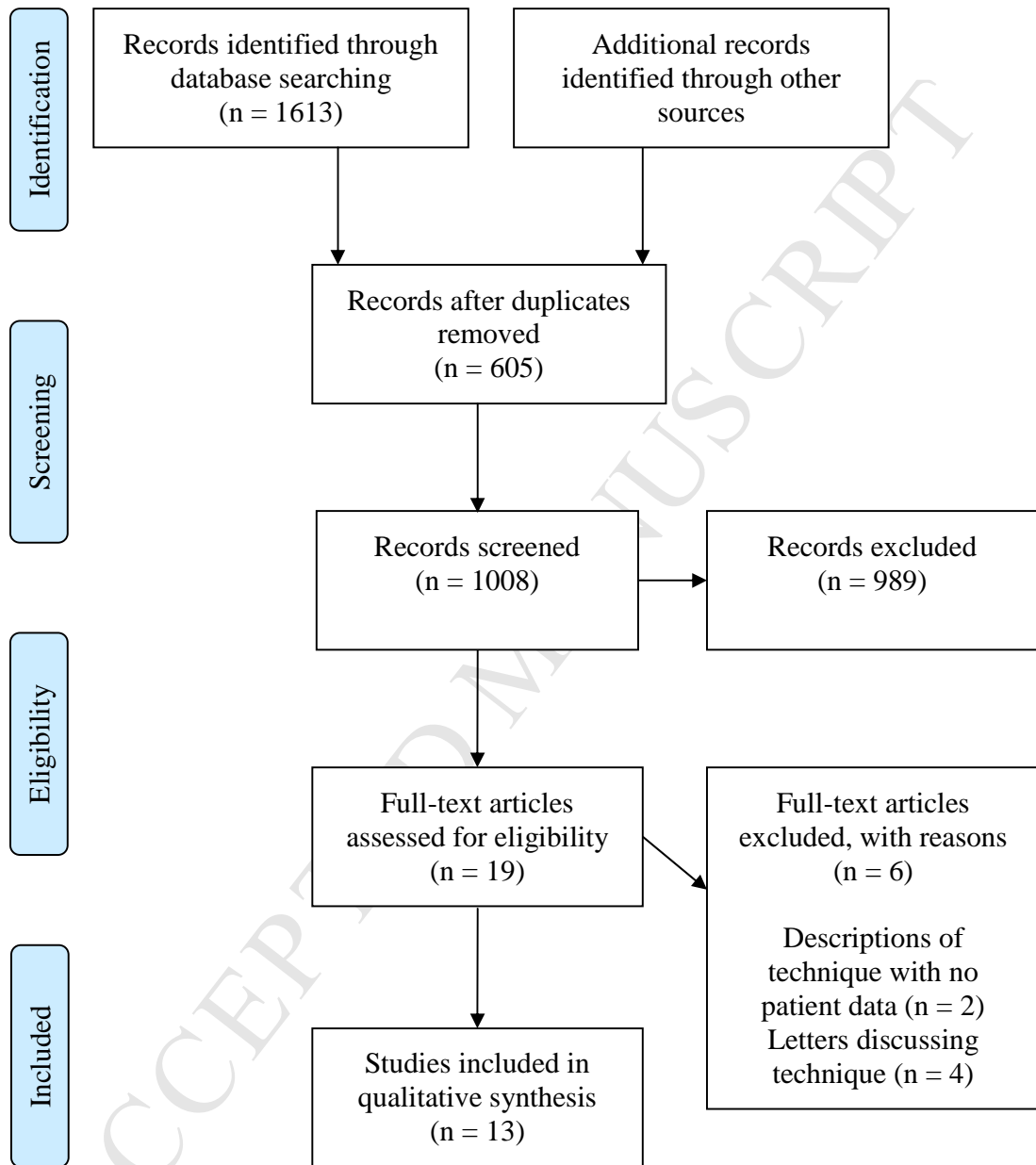
Lead author	Dysplasia	Rectal cancer	Other indications	Stage (histological)	Neo-adjuvant and adjuvant therapy	Resection margins
<i>Bricot [15] *</i>	-	-	-	-	-	-
Le Treut [4]	0	45/60	10 other cancer (exenteration) 5 benign: 4 adenomas; 1 Hirschsprung's disease	7 Dukes' A; 19 Dukes' B; 12 Dukes' C; 7 Dukes' D	Not stated	45 not stated
Abou-Zeid [5]	0	0/1	1 benign: Hartmann's reversal	n/a	n/a	n/a
Williams [11]	2	5/14	7 benign: 5 UC (4 dysplasia, 1 proctitis); 2 traumatic	3 T2N1M0; 2 T3N1M0	2 neo-adjuvant CRT 2 adjuvant chemotherapy	5 R0
Agrawal [16]	0	7/7	0	4 T2N1M0; 2 T3N0M0; 1 T3N1M0	0 neo-adjuvant 7 adjuvant chemotherapy	7 R0
Xiong [17]	0	12/12	0	Stage 1: 3; Stage 2a: 6; Stage 2b: 2; Stage 3: 1	Not stated	12 R0
<i>Qiu [23] *</i>	0	1/1	0	<i>T2N0M0</i>	<i>1 neo-adjuvant CRT</i>	<i>1 R0</i>
Qiu [20]	7	18/26	1 villous tubular adenoma	10 T2N0M0; 5 T3N0M0; 3 T3N1M0	14 neo-adjuvant CRT	18 R0
Marquardt [24]	0	1/1	0	T3N0M0	1 neo-adjuvant CRT	1 R0
Li [18]	0	39/39	0	Pre-op stage: 11 Dukes' A, 25 Dukes' B, 3 Dukes' C	Not stated	39 R0
Tong [22]	0	1/1	0	T2N0M0	1 neo-adjuvant CRT	1 R0
Wang [19]	0	8/8	0	Stage 1: 1; Stage 2: 4; Stage 3: 3	2 declined neo-adjuvant, 4 adjuvant chemotherapy	8 R0
Di Palo [21]	0	5/5	0	1 PCR 1 T2N0M0; 3 T3N+M0	Not stated	5 R0

Studies in italics and marked with * have results which are duplicated and the patients are not included in the numbers for analysis. Staging given is as described in each study. UC Ulcerative colitis, n/a not applicable, CRT chemotherapy and radiotherapy, PCR pathologic complete response

Table 3 Intra-operative and post-operative morbidity with the overall numbers of patients who developed each complication

Complications	Patients
Anastomotic leak	3
Colonic necrosis	1
Peritonitis	1
Haemorrhage	1
Intra-abdominal abscess	1
Intra-op injury to rectum	1
Splenectomy	1
Pelvic haematoma	1
Obstruction	2
Ileus	1
Pneumonia	2
Perineal infection	8
Perineal dehiscence	2
Fistula	
- Perineal	24
- Vaginal	2
Stricture	7
Erectile dysfunction	6

Figure 1. PRISMA flow diagram



Highlights

- APPEAR has comparable morbidity, mortality and short-term oncological outcomes with other techniques for low rectal resection.
- The permanent stoma rate was 8/155 (5%)
- Longer-term oncological and functional results are needed to fully determine the role of this procedure.