Systematic review

doi:10.1111/codi.13151

A systematic review of transanal total mesorectal excision: is this the future of rectal cancer surgery?

C. Simillis*, R. Hompes†, M. Penna†, S. Rasheed* and P. P. Tekkis*

*Department of Colorectal Surgery, Royal Marsden Hospital, London, UK and †Oxford University Hospitals NHS Foundation Trust, Churchill Hospital, Headington, Oxford, UK

Received 4 May 2015; accepted 21 September 2015; Accepted Article online 15 October 2015

Abstract

Aim The surgical technique used for transanal total mesorectal excision (TaTME) was reviewed including the oncological quality of resection and the peri-operative outcome.

Method A literature search of MEDLINE, Embase, Science Citation Index Expanded and Cochrane was performed in order to identify studies reporting on TaTME.

Results Thirty-six studies (eight case reports, 24 case series and four comparative studies) were identified, reporting 510 patients who underwent TaTME. The mean age ranged from 43 to 80 years and the mean body mass index from 21.7 to 31.8 kg/m^2. The mean distance of the tumour from the anal verge ranged from 4 to 9.7 cm. The mean operation time ranged from 143 to 450 min and mean operative blood loss from 22 to 225 ml. The ratio of hand-sewn coloanal to stapled anastomoses performed was 2:1. One death was reported and the peri-operative morbidity rate was 35%. The anastomotic leakage rate was 6.1% and the reoperation rate was 3.7%. The mean hospital stay ranged from 4.3 to 16.6 days. The mesorectal excision was described as complete in 88% cases, nearly complete in 6% and incomplete in 6%. The circumferential resection margin was negative in 95% of cases and the distal resection margin was negative in 99.7%.

Conclusion TaTME is a feasible and reproducible technique, with good quality of oncological resection. Standardization of the technique is required with formal training. Clear indications for this procedure need to be defined and its safety further assessed in future trials.

Keywords Transanal total mesorectal excision, transanal minimally invasive surgery, natural orifice transluminal endoscopic surgery, rectal cancer, systematic review

Introduction

Total mesorectal excision (TME) was first described in 1982 by Heald *et al.* [1] and since then it has been established as the gold standard treatment of middle and lower third rectal cancers. TME is based on the principle of excising the rectal tumour and the mesorectum *en bloc,* including its blood supply and lymphatic drainage, to optimize locoregional clearance. TME has classically been performed by an open anterior abdominal approach, but advances in technology and surgical technique have enabled TME to be performed using minimally invasive techniques.

Laparoscopic TME (LapTME) has been shown to give similar results to the classical open approach with regard to peri-operative morbidity, surgical margins, quality of the surgical specimen, number of resected lymph nodes, local recurrence and overall survival [2–7]. In addition, LapTME was found to be associated with fewer wound infections, reduced blood loss, shorter hospital length of stay, earlier return to normal diet and earlier return of bowel function [3,5–11]. Nevertheless, a high conversion rate from laparoscopic to open surgery is still being reported (0–34%) [2–4,6,8,10–13] with an associated increased morbidity and worse oncological results [10,13,14]. Robotic-assisted laparoscopic anterior resection has also been performed which has been shown to have a similar outcome to LapTME with regard to operation time, operative blood loss, peri-operative morbidity, length of hospital stay, number of lymph nodes harvested, resection margins and local recurrence [15–17].

More recently, a transanal technique for TME has been developed with promising results. In transanal

Correspondence to: Mr Roel Hompes, Department of Colorectal Surgery, Oxford University Hospitals NHS Trust, Churchill Hospital, Old Road, Headington, Oxford OX3 7LE, UK.
E-mail: roelhompes@gmail.com

total mesorectal excision (TaTME) the rectum is mobilized transanally in a retrograde fashion. The technique has become possible due to advances in transanal endoscopic microsurgery (TEM) [18], transanal abdominal transanal proctosigmoidectomy with coloanal anastomosis (TATA) [19–21], transanal minimally invasive surgery (TAMIS) [22] and natural orifice transluminal endoscopic surgery (NOTES). TEM was introduced in 1983 by Buess *et al.* for resection of rectal adenomas and early carcinomas through a wide bore rigid proctoscope [18]. The TATA approach was described by Marks *et al.* in 1984 as an effective sphincter-preservation operation to avoid a permanent colostomy for low-lying rectal cancers [19–21]. Atallah *et al.* [22] introduced TAMIS, which uses a single-incision laparoscopic port to gain endoscopic access to the rectal vault using laparoscopic instruments. NOTES allows surgical procedures via natural orifices, e.g. transoral (gastrotomy), transvaginal or transanal (transrectal or colotomy). Transanal NOTES applied to colorectal disease is intuitive and makes more sense than other access routes because the target organ for transluminal access houses the pathology. NOTES transanal endoscopic rectosigmoid resection was first performed by Whiteford *et al.* [23] in 2007 on a human cadaver.

Extensive experimental research demonstrated the feasibility and safety of the transanal access for colon and rectal resections initially on animal [24–29] and human cadaver models [30–37]. The knowledge and experience gained from animal and cadaver studies led to human clinical trials. From 2010, TaTME, with or without laparoscopic assistance, has been performed on patients with rectal cancer and has shown promising results [38–42]. Studies have demonstrated the feasibility of this technique also with transanal robotic assistance [43–45].

The aim of this systematic review is to provide an up-to-date literature review based on all the studies reporting on the use of TaTME and to assess the perioperative outcome and the oncological quality of resection. In particular, the review will critically evaluate the feasibility and safety of this new and promising surgical treatment for rectal cancer.

Method

Search strategy

A comprehensive literature search using a combination of free-text terms and controlled vocabulary when applicable was performed of the following databases: MEDLINE, Embase, Science Citation Index Expanded, and Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library. The search period was from 1 January 2007 to the latest date for this search, which was 8 December 2014. The following search headings were used: 'transanal', 'transanal minimally invasive surgery' or 'TAMIS', 'transanal endoscopic microsurgery' or 'TEM', 'natural orifice transluminal endoscopic surgery' or 'NOTES', combined with each of the terms 'total mesorectal excision', 'TME' and 'proctectomy'. The detailed search strategy is provided in Table S1. The 'related articles' function from PubMed was used to broaden the search, and all abstracts, studies and citations scanned were reviewed. The references of the identified studies were also searched to identify additional studies for inclusion. No restrictions were made based on language or publication status.

Inclusion criteria and data collection

Case reports, case series or comparative studies, performed prospectively or retrospectively, were considered for this systematic review. Only studies reporting on TaTME performed on live human subjects were considered for inclusion. Full text was sought for any references which were identified for potential inclusion and further selection for inclusion was made based on the full text. The following data were extracted from each study: first author, year of publication, hospital, country, inclusion and exclusion criteria, sample size, study design, participant characteristics [such as age, gender, body mass index (BMI), neoadjuvant therapy received], tumour characteristics (clinical stage, distance from the anal verge or dentate line, tumour size), surgical technique (transanal platform used, transabdominal approach, anastomosis performed, use of diverting stoma), operative outcome (operation time, operative blood loss, extraction site, intra-operative complications, conversion to open surgery), postoperative outcome (length of hospital stay, postoperative complications, reoperations), histopathology results (length of specimen extracted, TME description, circumferential and distal resection margins, lymph nodes harvested and pathological stage) and long-term outcome (survival and cancer recurrence).

Statistical analysis

Continuous variables were analysed and reported as

1. overall range from all the included studies, e.g. age range of all participants;
2. range of means or medians for an outcome of interest reported by the included studies, e.g. range of reported means for age;

3 the most frequent mean or median reported by the included studies, e.g. the most frequent mean age reported by the studies.

Binary or dichotomous variables were analysed and reported as

1 ratio of an outcome of interest, e.g. male to female ratio of the participants;
2 percentage of patients with event from total number of participants based on the studies reporting on the outcome of interest, e.g. percentage of T1 tumour stage among studies reporting on preoperative tumour stage.

Results

Eligible studies

Figure 1 shows the study flow diagram. Of 874 references identified through electronic searches of Science Citation Index Expanded (n = 377), Embase (n = 325), MEDLINE (n = 164) and CENTRAL (n = 8), 215 duplicates between databases were excluded. A further 579 clearly irrelevant references were excluded through screening titles and reading abstracts. Eighty references were retrieved for further assessment. Three more studies were identified for further assessment through scanning reference lists of the identified studies. This left 83 studies that were investigated in detail in full text [27–29,32–111]. Of these 83 references, after reviewing the studies in detail the following studies were excluded for the following reasons: 16 studies were review articles [47–50,55,62,66,69,71,73,75,85,88,93,94,107], 12 were abstracts of published case series already included in the analysis [56,59,60,65,86,87,91,97,98,100,102,110], six were articles describing the surgical technique or videos [51,68,72,83,99,103], six were reporting on TaTME performed on cadavers [32–37], three were describing TaTME performed on animals [27–29], two were describing the anatomy for TaTME [46,57] and one was reporting on a study protocol design for comparing TaTME with LapTME [77]. One case report [54] was excluded because the same patient was reported in a case series [43] published by the same group.

After all exclusions 36 studies [38–45,52,53,58,61,63,64,67,70,74,76,78–82,84,89,90,92,95,96,101,104–106,108,109,111] reporting on 627 participants (510 participants who underwent TaTME and 117 participants who underwent LapTME) fulfilled the selection criteria and were included in the systematic review. They comprised eight case reports reporting on eight patients [38–40,53,67,79,106,109], 24 case series reporting on 389 patients [41–45,52,58,61,63,70,74,76,80,81,84,89,90,92,95,96,101,105,108,111] and four comparative studies comparing 113 patients who underwent TaTME with 117 who underwent LapTME [64,78,82,104]. Included in the case series, there were eight published abstracts [44,63,74,80,81,89,92,96] and one unpublished abstract [70]. There were two published abstracts [78,82] included in the comparative studies. Table 1 is a summary of the patient characteristics, surgical technique and operative and postoperative outcome in all the included studies. A more detailed description of each study is given in Tables S2–S5. Table S2 shows the patient characteristics, surgical technique and operative and postoperative outcome of the case reports, Table S3 shows the outcome from the case series published as articles, Table S4 from the case series reported as abstracts and Table S5 from the comparative studies.

Patient characteristics

In all, 510 patients underwent TaTME. Rectal adenocarcinoma was the indication for surgery in all except for 16 patients with benign disease. The age of patients in the studies ranged from 23 to 87 years and the mean age ranged from 43 to 80 years with the most frequent mean age being 65 years. The overall male to female ratio, calculated from the studies reporting gender, was 2:1. The BMI ranged from 16 to 42 kg/m^2 and the mean BMI ranged from 21.7 to 31.8 kg/m^2, with the most frequent mean BMI being 26 kg/m^2. Based on the studies reporting on neoadjuvant therapy, 71% of participants received chemoradiotherapy, 7% received radiotherapy, 1% received chemotherapy and 21% received no neoadjuvant treatment.

The tumour characteristics, including preoperative tumour staging, tumour size and distance of the tumour from the anal verge or from the dentate line, are summarized in Tables S2–S5. The distance of the tumour from the anal verge ranged from 1 to 15 cm, and the means of the studies ranged from 4 to 9.7 cm with the most frequent mean distance being 5 cm from the anal verge. Tumour size ranged from 0.6 to 9.3 cm and the mean size ranged from 2.5 to 3.7 cm. Among studies reporting on preoperative (clinical) tumour stage, 6% of the participants were staged as T1, 21% as T2, 65% as T3 and 8% as T4. For preoperative lymph node staging, 2% of patients were staged as Nx, 52% as N0, 29% as N1 and 17% as N2.

Surgical technique

TaTME was performed purely transanally (pure transanal TaTME) [58,79,95,108,109] or with laparoscopic assistance (hybrid TaTME) [39–42,52,61,76,90,101,105,108]. Pure transanal TaTME was performed in 18 reported cases [58,79,95,108,109]. Where hybrid

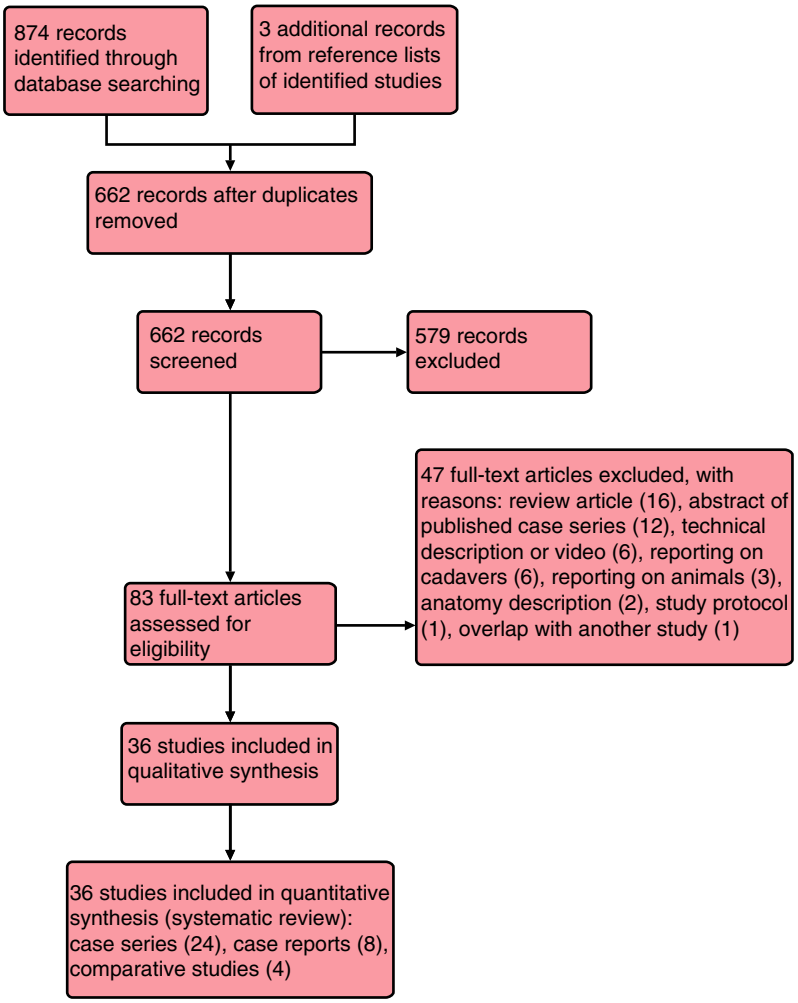

Figure 1 Study flow diagram.

TaTME was performed, laparoscopic assistance was provided through multiport laparoscopy (four or five ports) [42,43,84,90,95,101,106,108], mini-laparoscopy (three-port laparoscopy) [39,61,76,111] or single-port access [40,41,101,105]. For single-port laparoscopy the port was positioned in the planned ileostomy site. The ports reported to have been used for single-port laparoscopic assistance were Endorec Trocar (Aspide Medical, La Talaudiere, France) [40], GelPOINT (Applied Medical Inc., Rancho Santa Margarita, California, USA) [41] and SILS Port (Covidien, Mansfield, Massachusetts, USA) [105]. Multiport laparoscopy was performed using three ports [39,76,111] or more ports [39,42,61,76, 95]. Multiport laparoscopy with the da Vinci Robotic Surgical System–Si (Intuitive Surgical Inc., Sunnyvale, California, USA) was performed by some studies for the abdominal phase [43,45,67].

For hybrid TaTME, the abdominal portion of the operation can be completed laparoscopically, robotically, hand-assisted or with an open approach. During laparoscopy the abdomen and pelvis were inspected for tumour invasion of the peritoneum and to confirm the absence of dense pelvic adhesions and other factors that would preclude a proper dissection [61,95]. The splenic flexure was taken down laparoscopically, and the descending and sigmoid colon were mobilized. The sigmoid mesentery was divided with high ligation of the inferior mesenteric vessels [52,71,95]. Part of the superior rectal dissection could be initiated laparoscopically according to TME principles [71]. If the operating team consisted of an abdominal team and a perineal team, the abdominal and transanal phases during TaTME with laparoscopic assistance could be performed synchronously [64,95]. Synchronous two-team surgery has the potential to reduce the operation time [61,64,76,84] and allows the two teams to act synergistically by providing traction and countertraction [64] and by guiding each other to the correct dissection

Table 1 Summary of patient characteristics, surgical technique, operative and postoperative outcome of the included studies.

	N	Age*	Gender, M:F	Abdominal assistance†	Transanal platform†	OT* (min)	Intra-operative complications†	Postoperative complications†	LOS* (days)
Case reports published as articles									
Sylla *et al.* (2010) [39], Chen *et al.* (2010) [38], Tuech *et al.* (2011) [40], Leroy *et al.* (2013) [79], Zhang *et al.* (2013) [109], Gomez Ruiz *et al.* (2014) [67], Atallah *et al.* (2015) [53], Verheijen *et al.* (2014) [106]	8	57	3:5	ML {4}, none {2}, SL {1}, RL {1}	GelPOINT Path {3}, TEO proctoscope {2}, PPH {2}, Endorec {1}, *Robotic TaTME {2}	289	Rectal perforation {1}	Infected pelvic haematoma {1}	4.7
Case series published as articles									
Dumont *et al.* (2012) [41]	4	67	4:0	SL	GelPOINT Path	360	Intraperitoneal gas leak {1}	Anastomotic fistula {1}	13
Zorron *et al.* (2012) [42]	2	64	1:1	ML	Colonoscope {1}, single-port triport {1}	355	None	Transient feet paraesthesia {1}	7
Lacy *et al.* (2013) [76]	3	73	1:2	ML	GelPOINT Path	143	None	Dehydration – renal failure {1}	4.7
Lacy *et al.* (2013) [61]	20	65	11:9	ML	GelPOINT Path	235	None	Urinary retention {2}, ileus {1}, dehydration {1}	6.5
Rouanet *et al.* (2013) [90]	30	65	30:0	ML	TEO proctoscope	304	Conversion to open {2}, urethral injury {2}, air embolism {1}	Bowel obstruction {2}, peritonitis {1}, sepsis {1}, transient urinary disorder {2}, ***reoperation {2}**	14
Sylla *et al.* (2013) [95]	5	49	3:2	None {3}, ML {2}	TEO proctoscope	275	None	Ileus {1}, urinary retention {2}	5.2
Velthuis *et al.* (2013) [105]	5	69	3:2	SL	SILS Port	178	Pneumatosis of mesentery and retroperitoneum {1}	Ileus {1}, pneumonia {1}, presacral abscess {1}, ***reoperation {1}**	NR

Table I (Continued).

	N	Age*	Gender, M:F	Abdominal assistance†	Transanal platform†	OT* (min)	Intra-operative complications†	Postoperative complications†	LOS* (days)
Atallah *et al.* (2014) [52]	20	57	14:6	ML {11}, RL {6}, open {3}	GelPOINT Path, SILS Port	243	None	Wound infection {2}, anastomotic leak {1}, pelvic abscess {4}, ileus{4}, pneumonia{1}, renal failure {1}, perianastomotic fluid collection {2}, anastomotic stricture {4}, death due to pulmonary embolism 8 weeks post-op {1}, *reoperation {1}	4.5
Atallah *et al.* (2014) [43]	3	45	2:1	ML	GelPOINT Path, *Robotic TaTME	376	None	Peristomal dermatitis {1}, dehydration {1}, pulmonary embolism {1}	4.3
Chouillard *et al.* (2014) [58]	16	58	6:10	None {10}, SL {5}, ML {1}	GelPOINT Path, SILS Port	265	None	Small bowel obstruction in pelvis {1} and at diverting stoma {1}, pelvic abscess {1}, *reoperation {3}	10.4
Meng *et al.* (2014) [84]	3	80	2:1	ML	TEM rectoscope	365	None	None	6.5
Tuech *et al.* (2015) [101]	56	65	41:15	ML {43}, SL {8}, open {4}, RL {1}	Endorec Trocar {42}, SILS Port {11}, GelPOINT Path {3}	270	Conversion to open due to technical difficulties in obese patients {2} and due to adhesions {1}	Anastomotic leak {3}, pelvic sepsis without anastomotic leak {3} (2 needed CT-guided drainage), urinary retention {5}, blood transfusion {2}, cerebral infarction{1}	10

Table I (Continued).

	N	Age*	Gender, M:F	Abdominal assistance†	Transanal platform†	OT* (min)	Intra-operative complications†	Postoperative complications†	LOS* (days)
Wolthuis *et al.* (2014) [108]	14	65	5:9	ML {11}, none {3}	GelPOINT Path	148	Conversion to open {2}, inadequate exposure due to bleeding {1} or difficulty of maintaining insufflation {2}, rectal perforation {1}, difficult dissection due to fibrosis post-radiotherapy {1}	Transient fever {2}, urinary tract infection{3}, small pelvic haematoma {1}	8.7
Zorron *et al.* (2014) [111]	9	63	5:4	ML	Single-port triport {7}, colonoscope {2}	311	Conversion to open {1}, conversion to laparoscopic{1}	Transient feet paraesthesia {1}, anastomotic leak {1}, *reoperation {1}	7.6
Ruiz *et al.* (2015) [45]	5	53	4:1	RL	GelPOINT Path, *Robotic TaTME	375	None	Anastomotic leak {1}	6
Case series reported as abstracts									
Espin-Basany *et al.* (2014) [63]	20	71	17:3	NR	NR	NR	NR	Anastomotic leak {1}, presacral abscess{4}, *reoperation {3}	7
Kazieva *et al.* (2014) [74]	6	54	3:3	ML	Endoscopic TEM	243	NR	Anastomotic leak {4}, ileus {2}	12
Lezoche *et al.* (2014) [80]	8	66	5:3	ML	TEM rectoscope	450	None	Anastomotic leak {3}, urinary incontinence {1}, anastomotic stricture {2}, rectovaginal fistula {1} treated with stent	16.6
Malik *et al.* (2014) [81]	8	43	4:4	NR	NR	298	Pelvic bleeding treated by pelvic packs for 24 h {1}	Ileus {2}, high output stoma {1}, anastomotic stricture {1}	9
Rasulov *et al.* (2014) [89]	15	52	NR	ML	NR	302	NR	Urinary retention {3}	NR
Ruiz *et al.* (2014) [44]	8	62	5:3	RL	*Robotic TaTME	368	NR	Anastomotic leak {1}	5.5
Schirnhofer *et al.* (2014) [92]	9	69	6:3	SL	SILS Port, GelPOINT Path	243	Resection could not be completed {1}, conversion to open due to urethral injury{1}	NR	NR

Table I (Continued).

	N	Age*	Gender, M:F	Abdominal assistance†	Transanal platform†	OT* (min)	Intra-operative complications†	Postoperative complications†	LOS* (days)
Tasende *et al.* (2014) [96]	100	NR	NR	ML	NR	178	Pfannenstiel incision for specimen extraction {10}	Anastomotic leak {8}, other complications not reported	6
Hompes *et al.* (unpublished) [70]	20	NR	14:6	NR	NR	315	Conversions to open {3}	Complications {6} including pelvic haematoma {1}, anastomotic leak {1}	7
Comparative studies published as articles									
Velthuis *et al.* (2014) [104]	25	64	18:7	SL	SILS Port, GelPOINT Path	NR	NR	NR	NR
Fernandez-Hevia *et al.* (2015) [64]	37	65	24:13	ML	GelPOINT Path	215	NR	Anastomotic leak {2}, collection {1}, haemorrhage {1}, urinary retention {1}, ileus {4}, ascites {1}, fever {1}, high ileostomy output {1}, *reoperation {3}	6.8
Comparative studies published as abstracts									
Lelong *et al.* (2014) [78]	34	NR	NR	NR	NR	NR	Conversion to open {1}	Complications {9}	8
Marks *et al.* (2014) [82]	17	NR	NR	NR	NR	NR	NR	Complications {4}	NR
Overall	510	43–80	2:1	None {18}	Robotic TaTME {18}	143–450	9.6% (27/282),‡ urethral injury {3}	33.5% (126/376),‡ reoperation 3.7% (14/376)	4.3–16.6

For a more detailed description of each study please see Tables S2–S5.

LOS, length of stay; M:F, male:female; ML, multiport laparoscopy; *N*, number of participants; NR, not reported; OT, operation time; PPH, procedure for prolapsing haemorrhoids; RL, robotic laparoscopy; SL, single-port laparoscopy; TaTME, transanal total mesorectal excision; TEM, transanal endoscopic microsurgery; TEO, transanal endoscopic operation.

*Reported as a mean or median.

†{Number of participants}.

‡Based on the studies reporting on this outcome.

plane in a 'rendezvous' manner, i.e. meet each other from above and below [84]. Nevertheless, not every surgical department has the capability to perform TaTME synchronously as synchronous two-team surgery requires two separate nursing teams, two senior surgeons experienced in TaTME and two assistants.

Once the abdominal portion is completed, transanal TME is performed in most cases, but the operation could also begin with the transanal TME prior to entering the abdomen. Before the transanal phase begins, digital rectal examination, anoscopy or rigid proctoscopy is performed to confirm the location of the tumour and identify a safe distal margin [71,95]. For the transanal approach, a retractor was positioned for exposure and to circumferentially transect the distal rectum. To expose the lower rectum, a Lone Star retractor (Lone Star Medical Products Inc., Houston, Texas, USA) [41,43,58,61,95,108] may have been used, or a Scott ring retractor (Lone Star Medical Products, Stafford, Texas, USA) [104]. For low-lying tumours encroaching on the anorectal junction or located < 1.5 cm from the anorectal junction, a partial intersphincteric open dissection is performed under direct vision [52,71,95]. The mucosa and internal sphincter muscle are dissected circumferentially starting at least 1 cm below the distal margin of the tumour [95]. A purse-string suture is used for luminal occlusion of the rectum below the tumour and intersphincteric dissection is extended cephalad up to the level of the pelvic floor [52,61,71,95]. For tumours with a distal margin of more than 1.5 cm from the anorectal junction, the rectum is occluded with a circumferential rectal purse-string suture securing a safe distal margin (at least 1 cm below the lower tumour margin). This is done with the help of an anorectal retractor, or an anoscope, or proctoscope for exposure [52,95], or through the transanal platform [71]. Following rectal occlusion with the purse-string, the rectum is washed out with tumouricidal wash to prevent implantation of exfoliated tumour cells [71].

The transanal platform is then introduced transanally and the rectum is insufflated with CO_2 to a pressure of 9–15 mmHg [43,52,95]. Different transanal platforms have been used by the included studies such as a transanal endoscopic operation (TEO) proctoscope (Karl Storz, Tuttlingen, Germany) [39,79,90,95], Endorec Trocar (Aspide Medical) [39,79,90,95,101], GelPOINT Path Transanal Access Platform (Applied Medical) [41,43,53,58,61,76,106,108], transanal access port (PAT, Developia Inc., Spain) closed on the back with GelPOINT (Applied Medical) [45,67], SILS Port (Covidien) [52,105] and single-channel colonoscope (Olympus, Tokyo, Japan) [42,111]. The included studies demonstrated that TaTME can be performed using disposable flexible or reusable rigid platforms. There are currently no comparative data available between rigid and flexible transanal platforms. The rigid platforms are more costly as an initial investment, but may be cost-effective in the long term because they are reusable. Also, they provide a rigid stable platform for instrument manipulation and effective tissue retraction. With rigid platforms there is no need for a cameraman and the TEM scope has an integrated ventilator [95,112]. On the other hand disposable flexible platforms are pliable and allow for an adjusted fit within the anal canal and greater manoeuvrability [61,76]. In addition, disposable flexible platforms provide a less traumatic retraction possibly resulting in a less negative impact on anorectal function compared to rigid platforms [61,76]. The da Vinci Robotic Surgical System–Si (Intuitive Surgical) was used by some studies for the transanal resection and the robotic cart was side-docked parallel and as close as possible to the base of the operating table [43,45,67,106].

Standard laparoscopic instrumentation was used for rectal dissection and energy source devices reported to have been used were diathermy, the Harmonic Scalpel (Ethicon Endo-Surgery, Cincinnati, Ohio, USA) [95] or LigaSure (Covidien) [58]. The avascular presacral plane is identified when insufflated gas enters the tissue planes between the parietal endopelvic fascia and mesorectal envelope [71]. Posteriorly, the presacral plane is entered and the posterior dissection continued cephalad in the avascular presacral plane in accordance with TME principles [61,71]. The mesorectum is mobilized, and the plane of dissection extended medially and laterally [61,71]. Anteriorly, a plane on either side of Denonvilliers' fascia is chosen according to the location of the tumour, and the rectum is dissected from the posterior vagina or prostate until the peritoneal reflection is reached and opened [71,95]. The dissection then proceeds cephalad to communicate with the dissection performed laparoscopically from above. For pure TaTME, with no abdominal assistance, the left colon and the splenic flexure are mobilized transanally and the inferior mesenteric artery pedicle is divided transanally [58,95].

With completion of the mesorectal excision and with the colon adequately mobilized, the rectum is grasped and the colon exteriorized transanally [58,95,104]. The specimen can be extracted through the transanal platform if it is not bulky [71] or through an Alexis wound protector (Applied Medical) positioned transanally. Alternatively, if the specimen is too bulky a conventional abdominal extraction site and wound protector are used [71]. Proximal colonic resection is performed extracorporeally [61,95] and an anastomosis is performed transanally or with laparoscopic assistance [61,95].

The anastomoses performed have been end-to-end hand-sewn coloanal [39,41,43,45,52,58,61,95,108], side-to-end hand-sewn coloanal [40,79,101], end-to-end stapled [61,67,76,84,109], side-to-end stapled [61,76] and J-pouch anastomosis [52]. The double purse-string technique is used for stapled anastomosis [71]. From the studies reporting on the anastomotic technique 66% of the anastomoses have been hand-sewn coloanal and 34% were stapled, giving a ratio of hand-sewn coloanal to stapled anastomoses of 2:1. A diverting loop ileostomy is created in most cases unless a permanent stoma is to be fashioned [39,40,43,45,52,67, 104,106,111].

Operative details

The operation time ranged from 76 to 495 min, and the mean operative time reported by the included studies ranged from 143 to 450 min. The operative blood loss ranged from 0 to 600 ml, and the mean reported by the included studies ranged from 22 to 225 ml. Twelve conversions to open surgery were reported. The reasons given for nine of the conversions were posterior fixity of the tumour (two) [90], intra-abdominal adhesions after previous laparotomy (three) [101,108], a bulky and high tumour (one) [111], urethral injury (one) [92] and technical difficulties in an obese male patient (BMI 32) [101] and an obese female patient (BMI 37) [101].

Intra-operative complications included one small tear of the rectal wall which was sutured using the Endostich device inserted through the transanal platform [39], and a rectal perforation which occurred in a patient with known metastatic rectal cancer to liver and lung [108]. One study reported a case of intra-operative pelvic bleeding treated by pelvic packs for 24 h [81]. Other reported intra-operative complications were urethral injury (three) [90,92], two of which were sutured transanally [90] and oxygen desaturation with suspicion of air embolism in one case [90].

Wolthuis *et al.* [108] reported inadequate surgical field exposure due to the difficulty of maintaining insufflation (two cases) or due to bleeding (one case), which complicated the critical view to dissect safely in a cephalad direction. The same study reported difficult dissection on the Denonvilliers' fascia owing to fibrosis after radiotherapy for concurrent prostate cancer (one case) [108]. Dumont *et al.* [41] reported accidentally opening the peritoneum of the pouch of Douglas before completion of the middle lateral rectal dissection, and the transanal procedure had to be stopped because of leakage of intraperitoneal gas leading to low pelvic pressure with poor vision. Another study reported pneumatosis of the retroperitoneum and mesentery of the small bowel, making laparoscopic mobilization of the sigmoid difficult [104]. Finally, Tasende *et al.* [96] reported that a Pfannenstiel incision was required for specimen extraction in 10% of their cases due to bulky tumours.

Postoperative course

The length of postoperative hospital stay ranged from 2 to 29 days, and the mean length of hospital stay reported by the included studies ranged from 4.3 to 16.6 days. There was no 30-day mortality. A single death due to pulmonary embolism was reported 8 weeks postoperatively [52]. The anastomotic leakage rate was 6.1%. The peri-operative morbidity rate, including operative and postoperative morbidity, based on the studies that reported this outcome, was calculated to be 35%.

The following postoperative complications were reported by the included studies: anastomotic leakage (26 cases) [44,45,52,63,64,70,74,80,96,101,111], pelvic abscess formation (16 cases) [43,52,58,63,64,101, 104], urinary retention and transient urinary dysfunction (15 cases) [61,64,89,90,95,101], small bowel paralytic ileus (15 cases) [52,61,64,74,81,95,104], anastomotic stenosis (seven cases) [52,80,81], water and sodium depletion due to increased ileostomy output causing renal failure (five cases) [43,61,64,76,81], bowel obstruction (four cases) [58,90], pelvic haematoma formation (three cases) [70,79,108], urinary tract infection (three cases) [108], fever (three cases) [64,108], wound infection (two cases) [52], pneumonia (two cases) [52,104], transient paraesthesia of both feet due to intra-operative positioning (two cases) [42,111], red blood cell transfusion postoperatively (two cases) [101], pulmonary embolism 2 weeks postoperatively treated with systemic anticoagulation (one case) [43], pulmonary embolism 8 weeks postoperatively which led to the death of the patient (one case) [52], anastomotic fistula (one case) [41], sepsis requiring critical care (one case) [90], urinary incontinence (one case) [80], ascites (one case) [64], acute renal failure (one case) [52], rectovaginal fistula (one case) [80], haemorrhage (one case) [64], stoma dermatitis related to high output from diverting ileostomy (one case) [43], cerebral infarction with a favourable outcome (one case) [101] and peritonitis secondary to ileal injury without a direct link with the TaTME procedure (one case) [90]. Seventeen more cases were included in postoperative complications from studies which did not report the cause of morbidity in detail [70,78,82].

Some studies described the interventions required for management of the complications. One patient who developed an anastomotic stricture was successfully trea-

ted with dilatation [81], and one who developed a rectovaginal fistula was treated by stenting [80]. Two patients diagnosed with pelvic sepsis without evidence of anastomotic leakage required CT-guided drainage [101]. Fourteen reoperations were reported in total [52,58,63,64,90,105,111], giving a reoperation rate of 3.7%. From the studies that reported on the causes for reoperation, one presacral abscess was treated by repeated laparoscopic drainage [104] and another pelvic abscess without anastomotic leakage required reoperation [58]. Small bowel obstruction was the cause of reoperation in two cases, one occurring at the level of the diverting stoma and the other due to incarceration of a small bowel loop in the pelvis [58]. Two anastomotic leaks related to necrotic proximal colon due to ischaemia necessitated reoperation with dismantling of the coloanal anastomosis and construction of a permanent end colostomy [52,111].

Histopathological results

The number of lymph nodes harvested ranged from 5 to 81, with a mean ranging from 11.5 to 33. Among studies reporting on postoperative histopathological tumour stage, 11% of participants were staged as T0, 1% as Tis, 10% as T1, 26% as T2, 48% as T3 and 4% as T4. With regard to postoperative N stage, 72% of participants were staged as N0, 19% as N1 and 9% as N2.

From the 462 reports on the histopathological examination of the TME specimens, the mesorectal excision was described as complete (287 reports) or intact (26) or Grade 3 (42) or satisfactory (42) or adequate (eight) in 88% of cases, as nearly complete (22) or Grade 2 (seven) in 6% of cases, and as incomplete (23) or inadequate (three) or Grade 1 (two) in 6% of cases. From the 455 reports on the circumferential resection margin (CRM), this was negative with a distance between resection margin and tumour of more than 1 mm in 433 (95%) cases and was positive (i.e. tumour infiltration within 1 mm or less from the resection margin) in 22 (5%) cases. Regarding tumour at the distal resection margin (DRM), there were 326 reports in total, 325 of which were negative (99.7%) and one was positive (0.3%).

Follow-up

Six studies reported the follow-up after TaTME [52,58,78,90,95,101]. Rouanet *et al.* [90], with a median follow-up of 21 (10–41) months, reported four cancer-related deaths, including one due to an isolated locoregional recurrence and one caused by hepatic cirrhosis. The same authors also reported that 12 patients were treated for locoregional or distant recurrence, and four experienced locoregional recurrence alone. The reported overall survival rates at 12 and 24 months were 96.6% [95% confidence interval (CI) 78.0–99.5] and 80.5% (95% CI 53.0–92.9), and the recurrence-free survival rates at 12 and 24 months were 93.3% (95% CI 75.9–98.3) and 88.9% (95% CI 69.0–96.3) [90]. Furthermore, Atallah *et al.* [52] at a 6-month median follow-up reported no locoregional recurrence but one case with distant metastases. Sylla *et al.* [95] reported that at a mean follow-up of 5.4 ± 2.3 months all patients were disease-free. Chouillard *et al.* [58] followed their patients for 9 months and reported no recurrence, whether local or distant.

Tuech *et al.* [101] followed their patients for a median time of 29 (18–52) months and reported an overall survival rate of 96.4%. There were four patients in the study with synchronous liver metastases who underwent hepatic resection. Of these two died at 24 and 37 months of metastases, one was alive without recurrence and one with liver and lung metastases continued to be followed up [101]. Tuech *et al.* [101] also reported a 1.7% rate of local recurrence and a 5-year disease-free survival rate of 94.2%. Among the 52 patients with non-metastatic rectal cancer at diagnosis, this study reported two cases of metastatic and one of local recurrence [101]. The single case of local recurrence developed at 24 months postoperatively and affected one of three patients with a CRM of < 1 mm (R1 resection) [101]. In a comparative study published as an abstract, Lelong *et al.* [78] followed up their patients for a median time of 24 months. The study reported comparable survival rates between TaTME and LapTME, and local recurrence rates of 3% (one case) for TaTME and a 6% (two cases) for LapTME.

Discussion

The limitations of current surgical TME techniques

LapTME can be technically demanding in patients with a bulky or an advanced distal rectal tumour showing a poor response to neoadjuvant treatment. Pelvic exposure during LapTME is particularly restricted in male patients with a narrow pelvis and in obese patients [52,90,95]. Previous pelvic radiation can make laparoscopic pelvic dissection more difficult, and tumours located on the anterior rectal wall have an increased risk of inadequate oncological clearance [52,95]. The use of laparoscopic staplers in a narrow pelvis is difficult and the multiple firings of staples across the low rectum is of concern [58,69,71]. Difficulties in pelvic exposure and limitations of instrumentation can affect not only the dissection during LapTME but also the preservation

of autonomic pelvic nerves and the possibility of achieving a restorative procedure [71]. Moreover, conversion from LapTME to open surgery is reported to be required in 0–34% of cases due to local tumour invasion or tumour fixation, difficult dissection in a narrow male pelvis, poor vision, obesity, bulky tumour, low rectal tumour, previous irradiation, bleeding, rectal perforation, dilated small bowel, extensive or dense adhesions, and anastomotic failure [2–4,6,8,10–13]. Patients converted from LapTME to open resection are known to have a higher operative mortality and morbidity and worse oncological results, compared with patients having laparoscopic or open TME [10,13,14].

The advantages of TaTME

TaTME was developed to overcome technical difficulties associated with LapTME and open TME. It may address some of the difficult aspects of laparoscopic or open TME, such as exposure, rectal dissection, distal cross-stapling of the rectum and sphincter preservation [71,95]. During TaTME, visualization of the deep pelvis is improved, with unobstructed views of the presacral and perirectal planes [69,71,95]. Transanal dissection is facilitated by tissue distention by CO_2 and pneumodissection and tissue retraction can be performed effectively through the transanal platform [52,69,71,95]. TaTME facilitates dissection of the difficult distal part of the TME dissection in the narrow pelvis but also allows clear definition of safe, tumour-free, radial and longitudinal margins, and may be ideal in patients for whom a laparoscopic pelvic dissection may be difficult with the risk of inadequate oncological clearance [69,71,95]. In addition, the specimen can be exteriorized transanally with TaTME, whereas an abdominal incision is routinely required for specimen extraction with the LapTME technique [71,95].

Oncological quality of TaTME

The oncological quality of resection for TaTME is comparable to that of open and laparoscopic TME. In this systematic review, following TaTME the CRM was positive in 5% of cases and the DRM was positive in 0.3% of cases. The reported incidence of a positive CRM for open TME ranges from 1.3% to 18.1% [2–4,9–11,13,113,114] and for LapTME from 1.2% to 18.1% [2–4,9–11,13,113,114]. The reported positive DRM in the literature for open TME is 0% to 1.2% [2,3,114] and for LapTME is 0% to 1.3% [2,3,114]. Furthermore, the studies included in this systematic review described the mesorectal excision as complete in 88% of cases, as nearly complete in 6% of cases and as incomplete in 6% of cases. In a study by Penninckx *et al.* [114] mesorectal excision was reported as incomplete in 11.4% of open TME cases and in 13.2% of LapTME cases, as nearly complete in 28% and 24.8% respectively, and as complete in 60.6% and 62%. Moreover, the mean number of harvested lymph nodes with TaTME ranged from 11.5 to 33, which is comparable to the reported mean number of harvested lymph nodes during open TME (11–18 lymph nodes) and LapTME (5.5–17 lymph nodes) [2–4,9–12,114]. The possibility of publication bias in the results reported by the included studies, however, should be taken into consideration.

Peri-operative morbidity

The peri-operative morbidity rate of 35% for TaTME is comparable to that of 8.5–37% for open TME [13,113] and 6.0–40% for LapTME [13,113]. Included in the intra-operative morbidity were three cases of urethral injury [90,92], two of which were sutured transanally [90]. Urethral injury is a serious complication related specifically to TaTME and is uncommon during open TME, LapTME or robotic TME. During TaTME the prostate may be inadvertently pulled down into the plane of dissection resulting in a urethral injury. Reassuringly there were two cases (< 1%) of rectal perforation [39,108]. The rate of intra-operative rectal perforation reported by Penninckx *et al.* [114] was 9.4% for open TME and 6.2% for LapTME. Furthermore, with TaTME, there is an increase in the need for coloanal anastomosis with its associated morbidity. The ratio of hand-sewn coloanal to stapled anastomosis was 2:1. The most frequently reported postoperative complication of anastomotic leakage at 6.1% is comparable to the rates of 1.4–12% reported for open TME [2–4,13,113,115] and of 1.2–10% reported for LapTME [2–4,9,13,113,115].

Urinary and sexual dysfunction

The other most common complication reported was urinary retention and transient urinary dysfunction of about 5%. Sylla *et al.* [95] performed urodynamic testing on their two cases of urinary dysfunction, which demonstrated evidence of minimal detrusor activity consistent with parasympathetic nerve injury. Postoperative urinary and sexual dysfunctions resulting from direct or indirect injury to the pelvic hypogastric or the sacral splanchnic nerves are recognized complications of rectal resection [116,117]. After laparoscopic or open TME, the reported incidence of urinary dysfunction is 0–26% and that of sexual dysfunction is 11–38% [116,118–120]. TaTME provides improved pelvic visualization

with enhanced anatomical definition, allowing more accurate dissection through the presacral plane between the mesorectal and pelvic fascia, which may result in sparing of the autonomic nerves during mesorectal dissection and therefore a lower incidence of urinary and sexual dysfunction [59,69]. With the mean operation time ranging from 143 to 450 min the effects of constant anal dilatation for a prolonged period are not known and, given the risks of urgency and incontinence associated with rectal resection, it is important to ensure that TaTME does not have an additive effect on damaging the sphincter muscles [71].

Comparative studies

There have been four studies [64,78,82,104] which have compared TaTME with LapTME. Two were published only as abstracts and none was a randomized controlled trial (RCT). Velthuis *et al.* [104] compared the pathological quality of specimens from patients who underwent TaTME with those obtained after traditional LapTME and found a statistically significant difference in the number of specimens with a complete mesorectum in 96% of the TaTME group and 72% of the LapTME group. No differences between the groups were seen in the length of specimen or the state of the CRM or DRM [104]. Fernandez-Hevia *et al.* [64] observed no significant difference in the 30-day postoperative complication rate between TaTME (32%) and LapTME (51%) ($P = 0.16$). In the same study, the TaTME group was found to have a significantly lower early hospital readmission rate and a significantly shorter operating time compared with the LapTME group [64]. In the TaTME group coloanal anastomosis was performed significantly more frequently and the DRM was significantly longer [64]. The comparative study by Marks *et al.* [82], published as an abstract, demonstrated no significant difference in the peri-operative or histopathological outcome compared with standard LapTME. The other comparative study published as an abstract by Lelong *et al.* [78] demonstrated a more favourable short-term outcome for TaTME than LapTME, including a lower conversion rate and a shorter hospital stay, with a comparable oncological quality of resection. The same study also reported the intermediate-term outcome at a median follow-up of 24 months, and showed comparable rates of local recurrence and overall survival between TaTME and LapTME [78].

Prerequisite skills and training

The oncological quality of resection and the peri-operative outcome of TaTME are related to the learning curve of the surgeon. TaTME can be technically difficult particularly for surgeons not used to performing transanal procedures. For these reasons, it should only be performed by a colorectal surgeon with expertise in advanced colorectal surgery, intersphincteric resections, laparoscopic and minimally invasive approaches, and advanced transanal platforms, such as TEM, TEO or TAMIS [52,69,71,95]. To date, formal training for transanal TME has not been established, and many surgeons strongly advocate procedural training on animals and/or human cadavers before attempting the procedure on patients [52,95]. Large case series on human cadavers have demonstrated a significant improvement in specimen length and operation time with increasing experience [32] and this may be the actual learning curve. Expertise in robotic surgery is also valuable, because robotic TaTME has the added advantages of a magnified view in three dimensions and high definition, as well as the seven degrees of freedom provided by the robotic wristed instruments [43].

Indications and standardization of technique

At present, there is no consensus between colorectal surgeons on the patient selection criteria for TaTME, including indications and contraindications for this procedure. Based on the findings of this review, TaTME would be suitable for patients requiring low anterior resection for low and mid rectal tumours. TaTME would also be more suitable in male patients with a narrow pelvis and in patients with a high BMI. Patients with a T4 tumour or one with a threatened CRM and with possible sphincter involvement should not be candidates for TaTME. Furthermore, the technique for TaTME has to be standardized to allow a safe and responsible introduction and general dissemination of the technique. Our group is planning to use a Delphi methodology to achieve a consensus of surgeons experienced in TaTME to make recommendations on the patient selection criteria and surgical technique for TaTME.

Limitations of the current review and future studies

Based on the information reported by the studies included in this systematic review, TaTME, with or without laparoscopic assistance, is a feasible and reproducible technique. Nevertheless, the results of the current review are limited by the nature of the included studies which are mostly case reports and case series. Only four comparative studies [64,78,82,104] were included in the analysis, and two of these were published as abstracts. No RCTs have been published to

date. The oncological safety associated with TaTME needs to be validated, and future multicentre large sample RCTs are required to investigate further the perioperative, oncological and long-term outcome with respect to local recurrence and overall survival. Precise primary and secondary end-points to be investigated by an RCT have yet to be agreed. To ensure adequate numbers for evaluation of this new procedure, a UK registry has been set up to collect relevant and high quality data on TaTME [71], and these data should help further to determine the best primary and secondary end-points for an RCT. A study design by Lacy *et al.* [77] for a two-arm multicentre RCT comparing TaTME with LapTME suggested that oncological histopathological results (circumferential margin and mesorectal quality) and postoperative morbidity should be the primary outcome of the RCT, and time to first oral intake, length of hospital stay, postoperative pain and functional outcomes as the secondary outcomes.

TaTME is a new surgical technique with potential in the treatment of rectal cancer. This systematic review of the literature has shown that with or without laparoscopic assistance TaTME is feasible and reproducible. Negative circumferential and distal margins and quality of mesorectal excision are comparable to those achieved by current surgical techniques. Standardization of the technique is required with formal training. Multicentre RCTs with defined selection criteria and defined perioperative, pathological and long-term outcomes are required to evaluate the efficacy and safety of TaTME as a valid treatment for rectal cancer.

Conflicts of interest and source of funding

No conflicts of interest. No external funding.

References

1 Heald RJ, Husband EM, Ryall RD. The mesorectum in rectal cancer surgery – the clue to pelvic recurrence? *Br J Surg* 1982; **69:** 613–6.
2 Braga M, Frasson M, Vignali A, Zuliani W, Capretti G, Di Carlo V. Laparoscopic resection in rectal cancer patients: outcome and cost–benefit analysis. *Dis Colon Rectum* 2007; **50:** 464–71.
3 Lujan J, Valero G, Hernandez Q, Sanchez A, Frutos MD, Parrilla P. Randomized clinical trial comparing laparoscopic and open surgery in patients with rectal cancer. *Br J Surg* 2009; **96:** 982–9.
4 Ng SS, Leung KL, Lee JF, Yiu RY, Li JC, Hon SS. Long-term morbidity and oncologic outcomes of laparoscopic-assisted anterior resection for upper rectal cancer: ten-year results of a prospective, randomized trial. *Dis Colon Rectum* 2009; **52:** 558–66.
5 Qu C, Yuan RF, Huang J *et al.* Meta-analysis of laparoscopic versus open total mesorectal excision for middle and low rectal cancer. *Zhonghua Wei Chang Wai Ke Za Zhi* [Chinese J Gastrointest Surg] 2013; **16:** 748–52.
6 van der Pas MH, Haglind E, Cuesta MA *et al.* Laparoscopic versus open surgery for rectal cancer (COLOR II): short-term outcomes of a randomised, phase 3 trial. *Lancet Oncol* 2013; **14:** 210–8.
7 Vennix S, Pelzers L, Bouvy N *et al.* Laparoscopic versus open total mesorectal excision for rectal cancer. *Cochrane Database Syst Rev* 2014; (4): CD005200.
8 Breukink SO, van der Zaag-Loonen HJ, Bouma EM *et al.* Prospective evaluation of quality of life and sexual functioning after laparoscopic total mesorectal excision. *Dis Colon Rectum* 2007; **50:** 147–55.
9 Kang SB, Park JW, Jeong SY *et al.* Open versus laparoscopic surgery for mid or low rectal cancer after neoadjuvant chemoradiotherapy (COREAN trial): short-term outcomes of an open-label randomised controlled trial. *Lancet Oncol* 2010; **11:** 637–45.
10 Krane MK, Fichera A. Laparoscopic rectal cancer surgery: where do we stand? *World J Gastroenterol* 2012; **18:** 6747–55.
11 Ng SS, Leung KL, Lee JF *et al.* Laparoscopic-assisted versus open abdominoperineal resection for low rectal cancer: a prospective randomized trial. *Ann Surg Oncol* 2008; **15:** 2418–25.
12 Araujo SE, da Silva eSousa AH Jr, de Campos FG *et al.* Conventional approach × laparoscopic abdominoperineal resection for rectal cancer treatment after neoadjuvant chemoradiation: results of a prospective randomized trial. *Rev Hosp Clin Fac Med Sao Paulo* 2003; **58:** 133–40.
13 Guillou PJ, Quirke P, Thorpe H *et al.* Short-term endpoints of conventional versus laparoscopic-assisted surgery in patients with colorectal cancer (MRC CLASICC trial): multicentre, randomised controlled trial. *Lancet* 2005; **365:** 1718–26.
14 Poon JT, Law WL. Laparoscopic resection for rectal cancer: a review. *Ann Surg Oncol* 2009; **16:** 3038–47.
15 Gonzalez Fernandez AM, Mascarenas Gonzalez JF. [Total laparoscopic mesorectal excision versus robot-assisted in the treatment of rectal cancer: a meta-analysis]. *Cir Esp* 2012; **90:** 348–54.
16 Kang J, Yoon KJ, Min BS *et al.* The impact of robotic surgery for mid and low rectal cancer: a case-matched analysis of a 3-arm comparison – open, laparoscopic, and robotic surgery. *Ann Surg* 2013; **257:** 95–101.
17 Xiong B, Ma L, Zhang C, Cheng Y. Robotic versus laparoscopic total mesorectal excision for rectal cancer: a meta-analysis. *J Surg Res* 2014; **188:** 404–14.
18 Buess G, Theiss R, Hutterer F *et al.* [Transanal endoscopic surgery of the rectum – testing a new method in animal experiments]. *Leber Magen Darm* 1983; **13:** 73–7.
19 Bannon JP, Marks GJ, Mohiuddin M, Rakinic J, Jian NZ, Nagle D. Radical and local excisional methods of sphincter-sparing surgery after high-dose radiation for cancer of

the distal 3 cm of the rectum. *Ann Surg Oncol* 1995; **2:** 221–7.
20 Marks GJ, Marks JH, Mohiuddin M, Brady L. Radical sphincter preservation surgery with coloanal anastomosis following high-dose external irradiation for the very low lying rectal cancer. *Recent Results Cancer Res* 1998; **146:** 161–74.
21 Marks J, Mizrahi B, Dalane S, Nweze I, Marks G. Laparoscopic transanal abdominal transanal resection with sphincter preservation for rectal cancer in the distal 3 cm of the rectum after neoadjuvant therapy. *Surg Endosc* 2010; **24:** 2700–7.
22 Atallah S, Albert M, Larach S. Transanal minimally invasive surgery: a giant leap forward. *Surg Endosc* 2010; **24:** 2200–5.
23 Whiteford MH, Denk PM, Swanstrom LL. Feasibility of radical sigmoid colectomy performed as natural orifice translumenal endoscopic surgery (NOTES) using transanal endoscopic microsurgery. *Surg Endosc* 2007; **21:** 1870–4.
24 Sohn DK, Jeong SY, Park JW *et al.* Comparative study of NOTES rectosigmoidectomy in a swine model: E-NOTES vs. P-NOTES. *Endoscopy* 2011; **43:** 526–32.
25 Sylla P, Sohn DK, Cizginer S *et al.* Survival study of natural orifice translumenal endoscopic surgery for rectosigmoid resection using transanal endoscopic microsurgery with or without transgastric endoscopic assistance in a swine model. *Surg Endosc* 2010; **24:** 2022–30.
26 Sylla P, Willingham FF, Sohn DK, Gee D, Brugge WR, Rattner DW. NOTES rectosigmoid resection using transanal endoscopic microsurgery (TEM) with transgastric endoscopic assistance: a pilot study in swine. *J Gastrointest Surg* 2008; **12:** 1717–23.
27 Araujo SE, Seid VE, Horcel LA. Transanal endoscopic proctectomy: a case in swine. *Hepatogastroenterology* 2014; **61:** 333–5.
28 Park SJ, Sohn DK, Chang TY *et al.* Transanal natural orifice translumenal endoscopic surgery total mesorectal excision in animal models: endoscopic inferior mesenteric artery dissection made easier by a retroperitoneal approach. *Ann Surg Treat Res* 2014; **87:** 1–4.
29 Trunzo JA, Delaney CP. Natural orifice proctectomy using a transanal endoscopic microsurgical technique in a porcine model. *Surg Innov* 2010; **17:** 48–52.
30 Bhattacharjee HK, Kirschniak A, Storz P, Wilhelm P, Kunert W. Transanal endoscopic microsurgery-based transanal access for colorectal surgery: experience on human cadavers. *J Laparoendosc Adv Surg Tech A* 2011; **21:** 835–40.
31 Fajardo AD, Hunt SR, Fleshman JW, Mutch MG. Video. Transanal single-port low anterior resection in a cadaver model. *Surg Endosc* 2010; **24:** 1765.
32 Telem DA, Han KS, Kim MC *et al.* Transanal rectosigmoid resection via natural orifice translumenal endoscopic surgery (NOTES) with total mesorectal excision in a large human cadaver series. *Surg Endosc* 2013; **27:** 74–80.
33 Gomez Ruiz M, Martin Parra I, Calleja Iglesias A *et al.* Preclinical cadaveric study of transanal robotic proctectomy with total mesorectal excision combined with laparoscopic assistance. *Int J Med Robot* 2015; **11:** 188–93.
34 McLemore EC, Coker AM, Devaraj B *et al.* TAMIS-assisted laparoscopic low anterior resection with total mesorectal excision in a cadaveric series. *Surg Endosc* 2013; **27:** 3478–84.
35 Park JW, Kim YS, Sohn DK *et al.* Natural orifice total mesorectal excision using transanal port combined with singleport laparoscopy through stoma site: lessons from a cadaveric study. *Surg Endosc* 2013; **27:** S461.
36 Sylla P, Kim M, Dursun A *et al.* NOTES rectosigmoid resection using transanal endoscopic microsurgery (TEM): experience in human cadavers. *Dis Colon Rectum* 2010; **53:** 640.
37 Telem DA, Han KS, Kim MC *et al.* NOTES transanal rectosigmoid resection with total mesorectal excision in a large human cadaver series. *Surg Endosc* 2012; **26:** S212.
38 Chen Y, Hu M, Lei J, Chen J, Li J. Transanal endoscopic total mesorectal excision in the treatment of rectal cancer. *Endoscopy* 2010; **16:** 1261–5.
39 Sylla P, Rattner DW, Delgado S, Lacy AM. NOTES transanal rectal cancer resection using transanal endoscopic microsurgery and laparoscopic assistance. *Surg Endosc* 2010; **24:** 1205–10.
40 Tuech JJ, Bridoux V, Kianifard B *et al.* Natural orifice total mesorectal excision using transanal port and laparoscopic assistance. *Eur J Surg Oncol* 2011; **37:** 334–5.
41 Dumont F, Goere D, Honore C, Elias D. Transanal endoscopic total mesorectal excision combined with single-port laparoscopy. *Dis Colon Rectum* 2012; **55:** 996–1001.
42 Zorron R, Phillips HN, Coelho D, Flach L, Lemos FB, Vassallo RC. Perirectal NOTES access: 'down-to-up' total mesorectal excision for rectal cancer. *Surg Innov* 2012; **19:** 11–9.
43 Atallah S, Martin-Perez B, Pinan J *et al.* Robotic transanal total mesorectal excision: a pilot study. *Tech Coloproctol* 2014; **18:** 1047–53.
44 Ruiz MG, Palazuelos CM, Parra IM *et al.* Robotic transanal total mesorectal excision with laparoscopic assistance for rectal cancer treatment. *Colorectal Dis* 2014; **16:** 68.
45 Ruiz MG, Parra IM, Palazuelos CM *et al.* Robotic-assisted laparoscopic transanal total mesorectal excision for rectal cancer: a prospective pilot study. *Dis Colon Rectum* 2015; **58:** 145–53.
46 Aigner F, Hormann R, Fritsch H *et al.* Anatomical considerations for transanal minimal-invasive surgery – the caudal to cephalic approach. *Colorectal Dis* 2014; **16:** 57.
47 Al-Furaji HH, Sehgal R, Mansoor T, Burke J, Cahill RA. Transanal and transrectal operations for excisional surgery of the low and mid rectum (with video). *Surg Technol Int* 2014; **XXIV:** 124–32.
48 Araujo SE, Crawshaw B, Mendes CR, Delaney CP. Transanal total mesorectal excision: a systematic review of the experimental and clinical evidence. *Tech Coloproctol* 2015; **19:** 69–82.
49 Atallah S. Transanal minimally invasive surgery for total mesorectal excision. *Minim Invasive Ther Allied Technol* 2014; **23:** 10–6.

50 Atallah S, Albert M, deBeche-Adams T, Larach S. Transanal minimally invasive surgery (TAMIS): applications beyond local excision. *Tech Coloproctol* 2013; **17:** 239–43.

51 Atallah S, Albert M, deBeche-Adams T, Nassif G, Polavarapu H, Larach S. Transanal minimally invasive surgery for total mesorectal excision (TAMIS-TME): a stepwise description of the surgical technique with video demonstration. *Tech Coloproctol* 2013; **17:** 321–5.

52 Atallah S, Martin-Perez B, Albert M *et al.* Transanal minimally invasive surgery for total mesorectal excision (TAMIS-TME): results and experience with the first 20 patients undergoing curative-intent rectal cancer surgery at a single institution. *Tech Coloproctol* 2014; **18:** 473–80.

53 Atallah S, Nassif G, Larach S. Stereotactic navigation for TAMIS-TME: opening the gateway to frameless, image-guided abdominal and pelvic surgery. *Surg Endosc* 2015; **29:** 207–11.

54 Atallah S, Nassif G, Polavarapu H *et al.* Robotic-assisted transanal surgery for total mesorectal excision (RATS-TME): a description of a novel surgical approach with video demonstration. *Tech Coloproctol* 2013; **17:** 441–7.

55 Atallah SB, Larach S, deBeche-Adams TC, Albert MR. Transanal minimally invasive surgery (TAMIS): a technique that can be used for retrograde proctectomy. *Dis Colon Rectum* 2013; **56:** 931.

56 Bertrand M, Rouanet P, Mourregot A *et al.* Transanal endoscopic proctectomy (TAEP): an innovative procedure for difficult resection of rectal tumors in men with narrow pelvis. *Eur J Surg Oncol* 2012; **38:** 755–6.

57 Bertrand MM, Colombo PE, Alsaid B, Prudhomme M, Rouanet P. Transanal endoscopic proctectomy and nerve injury risk: bottom to top surgical anatomy, key points. *Dis Colon Rectum* 2014; **57:** 1145–8.

58 Chouillard E, Chahine E, Khoury G *et al.* NOTES total mesorectal excision (TME) for patients with rectal neoplasia: a preliminary experience. *Surg Endosc* 2014; **28:** 3150–7.

59 Chouillard EK. Transperineal NOTES-inspired approach to the total mesorectal excision (TME) in patients with rectal neoplasia: a preliminary experience. *Surg Endosc* 2014; **28:** 243.

60 Chouillard EK, Bonnet BV, Chahine E, Fingerhut AL. NOTES inspired approach to the mesorectum in patients with mid or low rectal cancer: a preliminary experience. *Surg Endosc* 2013; **27:** S476.

61 de Lacy AM, Rattner DW, Adelsdorfer C *et al.* Transanal natural orifice transluminal endoscopic surgery (NOTES) rectal resection: 'down-to-up' total mesorectal excision (TME) – short-term outcomes in the first 20 cases. *Surg Endosc* 2013; **27:** 3165–72.

62 Emhoff IA, Lee GC, Sylla P. Transanal colorectal resection using natural orifice translumenal endoscopic surgery (NOTES). *Dig Endosc* 2014; **26:** 29–42.

63 Espin-Basany E, Vallribera F, Jimenez LM *et al.* Transanal total mesorectal excision (TaTME). Short term results in low rectal carcinoma. *Colorectal Dis* 2014; **16:** 67.

64 Fernandez-Hevia M, Delgado S, Castells A *et al.* Transanal total mesorectal excision in rectal cancer: short-term outcomes in comparison with laparoscopic surgery. *Ann Surg* 2015; **261:** 221–7.

65 Fernandez-Hevia M, Delgado S, Tasende M *et al.* Transanal total mesorectal excision in rectal cancer. Short-term outcomes in comparison with laparoscopic surgery. *Colorectal Dis* 2014; **16:** 26.

66 Gomez Fleitas M. From Miles' procedure to robotic transanal proctectomy. *Cir Esp* 2014; **92:** 507–9.

67 Gomez Ruiz M, Palazuelos CM, Martin Parra JI *et al.* New technique of transanal proctectomy with completely robotic total mesorectal excision for rectal cancer. *Cir Esp* 2014; **92:** 356–61.

68 Grieco M, Abboud EC, Williams JR, Rasheid SH, Marcet J, Sanchez JE. Transanal minimally invasive surgery for total mesorectal excision (TAMISTME) with laparoscopic assistance. *Gastroenterology* 2014; **1:** S-1033.

69 Heald RJ. A new solution to some old problems: transanal TME. *Tech Coloproctol* 2013; **17:** 257–8.

70 Buchs NC, Nicholson GA, Yeung T *et al.* Transanal rectal resection: an initial experience of 20 cases. *Colorectal Dis* 2015, doi: 10.1111/codi.13227.

71 Hompes R, Arnold S, Warusavitarne J. Towards the safe introduction of transanal total mesorectal excision: the role of a clinical registry. *Colorectal Dis* 2014; **16:** 498–501.

72 Hompes R, Guy R, Jones O, Lindsey I, Mortensen N, Cunningham C. Transanal total mesorectal excision with a side-to-end stapled anastomosis – a video vignette. *Colorectal Dis* 2014; **16:** 567.

73 Kala Z, Skrovina M, Prochazka V, Grolich T, Klos k. [Transanal total mesorectal excision for rectal cancer – just a fashion trend?]. *Rozhl Chir* 2014; **93:** 564–7.

74 Kazieva L, Rybakov E, Chernyshov S, Aleshin D. Transanal endoscopic total mesorectal excision with laparoscopic assistance for low rectal carcinoma. *Colorectal Dis* 2014; **16:** 72.

75 Lacy AM, Adelsdorfer C. Totally transrectal endoscopic total mesorectal excision (TME). *Colorectal Dis* 2011; **13:** 43–6.

76 Lacy AM, Adelsdorfer C, Delgado S, Sylla P, Rattner DW. Minilaparoscopy-assisted transrectal low anterior resection (LAR): a preliminary study. *Surg Endosc* 2013; **27:** 339–46.

77 Lacy AM, Espin E, Biondo S *et al.* Transanal total mesorectal excision versus laparoscopic total mesorectal excision. Randomized study comparing 30-day postoperative morbidity. *Colorectal Dis* 2014; **16:** 106.

78 Lelong B, Mege D, Meillat H, Fara R, Delpero JR, De Chaisemartin C. Endoscopic transanal or laparoscopic transabdominal mesorectal excision for low rectal cancer: a single institutional case–control study. *Colorectal Dis* 2014; **16:** 8.

79 Leroy J, Barry BD, Melani A, Mutter D, Marescaux J. No-scar transanal total mesorectal excision the last step to pure NOTES for colorectal surgery. *JAMA Surg* 2013; **148:** 226–30.

80 Lezoche G. Transanal endoluminal total mesorectal resection (TETMR) by transanal endoscopic microsurgery (TEM) for the treatment of low rectal cancer. *Surg Endosc* 2014; **28:** S183.

81 Malik A, Arnold S, Venkatsubramanian A, Cecil T, Moran B. Transanal rectal resection (TARR): a novel and evolving technique in the operative management of low rectal pathology. *Colorectal Dis* 2014; **16:** 142.

82 Marks JH, Montenegro GA, Shields M, Marks G. Evolution of colorectal NOTES surgery: bottoms up transabdominal transanal (TATA)/total mesorectal excision (TME): a case matched study of transanal TME surgery for rectal cancer. *J Am Coll Surg* 2014; **1:** e72–83.

83 McLemore EC, Harnsberger CR, Sylla P *et al.* Transanal total mesorectal excision for rectal cancer: a training pathway. *Surg Endosc* 2014; **28:** 301.

84 Meng W, Lau K. Synchronous laparoscopic low anterior and transanal endoscopic microsurgery total mesorectal resection. *Minim Invasive Ther Allied Technol* 2014; **23:** 70–3.

85 Nahar Al-Furaji HH, Sehgal R, Mansoor T, Burke J, Cahill RA. Transanal and transrectal operations for excisional surgery of the low and mid rectum (with video). *Surg Technol Int* 2014; **24:** 124–32.

86 Nassif G, Polavarapu H, deBeche-Adams T, Atallah S, Albert M, Larach S. TAMIS total mesorectal excision for distal rectal cancer: early experience with short-term outcomes. *Dis Colon Rectum* 2013; **56:** E223–4.

87 Nassif GJ, Polavaropu H, Monroy A *et al.* Application of the TAMIS platform for complete pelvic resection. *Surg Endosc* 2013; **27:** S301.

88 Nieuwenhuis DH, Velthuis S, Bonjer J, Sietses C. Transanal total mesorectal excision: a new treatment option for rectal cancer [Transanale totale mesorectale excisie: Een nieuwe behandeling voor het rectumcarcinoom]. *Ned Tijdschr Geneeskd* 2014; **158:** A7054.

89 Rasulov A, Mamedli Z, Kulushev V *et al.* Transanal total mesorectal excision TEO-TME with N.O.S.E. and laparoscopic assistance for rectal cancer – preliminary results. *Colorectal Dis* 2014; **16:** 84.

90 Rouanet P, Mourregot A, Azar CC *et al.* Transanal endoscopic proctectomy: an innovative procedure for difficult resection of rectal tumors in men with narrow pelvis. *Dis Colon Rectum* 2013; **56:** 408–15.

91 Ruiz MG, Palazuelos CM, Parra JIM *et al.* New technique of transanal proctectomy with completely robotic total mesorectal excision for rectal cancer. *Cir Esp* 2014; **92:** 356–61.

92 Schirnhofer J, Brunner E, Mittermair C *et al.* Technical issues in transanal minimal invasive surgery: total mesorectal excision (TAMIS-TME). *Eur Surg* 2014; **46:** S58.

93 Serra-Aracil X. Transanal total mesorectal excision. *Cir Esp* 2014; **92:** 221–2.

94 Sylla P. Current experience and future directions of completely NOTES colorectal resection. *World J Gastrointest Surg* 2010; **2:** 193–8.

95 Sylla P, Bordeianou LG, Berger D *et al.* A pilot study of natural orifice transanal endoscopic total mesorectal excision with laparoscopic assistance for rectal cancer. *Surg Endosc* 2013; **27:** 3396–405.

96 Tasende M, Delgado S, De Lacy B *et al.* Transanal total mesorectal excision for rectal cancer: short-term outcomes after 100 cases. *Colorectal Dis* 2014; **16:** 14.

97 Tuech JJ, Bridoux V, Kianifard B *et al.* Natural orifice total mesorectal excision using transanal port and laparoscopic assistance. *Eur J Surg Oncol* 2010; **36:** 806–7.

98 Tuech JJ, Karoui M, Bridoux V, Kianifard B, Schwarz L, Michot F. Natural orifice proctectomy with total mesorectal excision using transanal port and laparoscopic assistance. *Surg Endosc* 2012; **26:** S179.

99 Tuech JJ, Karoui M, Bridoux V, Manceau G, Kianifard B, Michot F. Endoscopic trans anal proctectomy (ETAP): step by step surgical technique. *Surg Endosc* 2013; **27:** S189.

100 Tuech JJ, Karoui M, Bridoux V, Manceau G, Kianifard B, Michot F. A step towards NOTES total mesorectal excision for rectal cancer: endoscopic trans anal proctectomy (ETAP). *Surg Endosc* 2013; **27:** S28.

101 Tuech JJ, Karoui M, Lelong B *et al.* A step toward NOTES total mesorectal excision for rectal cancer: endoscopic transanal proctectomy. *Ann Surg* 2015; **261:** 228–33.

102 Tuech JJ, Karoui M, Lelong B *et al.* A step towards NOTES total mesorectal excision for rectal cancer: endoscopic transanal proctectomy (ETAP). *Colorectal Dis* 2014; **16:** 17.

103 Valverde A, Goasguen N, Oberlin O, Mosnier H. Video-assisted transanal proctectomy using the SILS monotrocar. *J Visc Surg* 2013; **150:** 33–43.

104 Velthuis S, Nieuwenhuis DH, Ruijter TE, Cuesta MA, Bonjer HJ, Sietses C. Transanal versus traditional laparoscopic total mesorectal excision for rectal carcinoma. *Surg Endosc* 2014; **28:** 3494–9.

105 Velthuis S, van den Boezem PB, van der Peet DL, Cuesta MA, Sietses C. Feasibility study of transanal total mesorectal excision. *Br J Surg* 2013; **100:** 828–31.

106 Verheijen PM, Consten EC, Broeders IA. Robotic transanal total mesorectal excision for rectal cancer: experience with a first case. *Int J Med Robot* 2014; **10:** 423–6.

107 Wexner SD, Berho M. Transanal TAMIS total mesorectal excision (TME) – a work in progress. *Tech Coloproctol* 2014; **18:** 423–5.

108 Wolthuis AM, De Buck Van Overstraeten A, D'Hoore A. Dynamic article: transanal rectal excision: a pilot study. *Dis Colon Rectum* 2014; **57:** 105–9.

109 Zhang H, Zhang YS, Jin XW, Li MZ, Fan JS, Yang ZH. Transanal single-port laparoscopic total mesorectal excision in the treatment of rectal cancer. *Tech Coloproctol* 2013; **17:** 117–23.

110 Zorron R, Neubarth H, Quintas C *et al.* Preliminary clinical experience on transcolonic NOTES – transrectal single port for rectal resection and TME. *Surg Endosc* 2011; **25:** S199.

111 Zorron R, Phillips HN, Wynn G, Neto MPG, Coelho D, Vassallo RC. Down-to-up transanal NOTES total mesorec-

tal excision for rectal cancer: preliminary series of 9 patients. *J Minim Access Surg* 2014; **10:** 144–50.
112 Telem DA, Berger DL, Bordeianou LG, Rattner DW, Sylla P. Update on transanal NOTES for rectal cancer: transitioning to human trials. *Minim Invasive Surg* 2012; **2012:** 287613.
113 Gong J, Shi DB, Li XX, Cai SJ, Guan ZQ, Xu Y. Short-term outcomes of laparoscopic total mesorectal excision compared to open surgery. *World J Gastroenterol* 2012; **18:** 7308–13.
114 Penninckx F, Kartheuser A, Van de Stadt J *et al.* Outcome following laparoscopic and open total mesorectal excision for rectal cancer. *Br J Surg* 2013; **100:** 1368–75.
115 Zhou ZG, Hu M, Li Y *et al.* Laparoscopic versus open total mesorectal excision with anal sphincter preservation for low rectal cancer. *Surg Endosc* 2004; **18:** 1211–5.
116 Kim NK, Aahn TW, Park JK *et al.* Assessment of sexual and voiding function after total mesorectal excision with pelvic autonomic nerve preservation in males with rectal cancer. *Dis Colon Rectum* 2002; **45:** 1178–85.
117 Morino M, Parini U, Allaix ME, Monasterolo G, Brachet Contul R, Garrone C. Male sexual and urinary function after laparoscopic total mesorectal excision. *Surg Endosc* 2009; **23:** 1233–40.
118 Maurer CA. Urinary and sexual function after total mesorectal excision. *Recent Results Cancer Res* 2005; **165:** 196–204.
119 Pocard M, Zinzindohoue F, Haab F, Caplin S, Parc R, Tiret E. A prospective study of sexual and urinary function before and after total mesorectal excision with autonomic nerve preservation for rectal cancer. *Surgery* 2002; **131:** 368–72.
120 Quah HM, Jayne DG, Eu KW, Seow-Choen F. Bladder and sexual dysfunction following laparoscopically assisted and conventional open mesorectal resection for cancer. *Br J Surg* 2002; **89:** 1551–6.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Detailed search strategy.

Table S2. Patient characteristics, surgical technique, operative and postoperative outcomes of published case reports.

Table S3. Patient characteristics, surgical technique, operative and postoperative outcomes of case series published as articles.

Table S4. Patient characteristics, surgical technique, operative and postoperative outcomes of case series reported as abstracts.

Table S5. Patient characteristics, surgical technique, operative and postoperative outcomes of published comparative studies.