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Beyond taTME: short-term outcomes of taTME in locally advanced rectal cancer requiring resection beyond total mesorectal excision

Short title: *taTME beyond total mesorectal excision*

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ABSTRACT

Aim:

To define the role of transanal total mesorectal excision (taTME) in locally advanced rectal cancer (LARC) requiring resection beyond the mesorectal plane.

Methods:

Retrospective review of the outcomes of a case series of patients undergoing taTME for rectal cancer with mesorectal fascia or adjacent organ involvement, .

Results:

Eleven patients (6 males) underwent transanal total mesorectal excision (taTME) for locally advanced rectal cancer requiring resection beyond total mesorectal excision. All had a restorative procedure. The transabdominal approach was open in five and minimally invasive in six cases. All patients required the resection of at least one adjacent structure including presacral fascia, internal iliac vessels, nerve roots, uterus, vagina or seminal vesicles. Four patients required a pelvic side-wall lymph node dissection and four had intraoperative radiotherapy. In all cases, the transanal approach was useful to disconnect the rectum distally, resect adjacent organs, or control the R1 risk-point. Three patients had Clavien-Dindo ≥ III or more complications (one mechanical bowel obstruction, one pelvic collection and one urine sepsis). There were no anastomotic complications. Ten patients had an R0 resection. During a median follow-up of 11 (8.6-16) months, there were no local recurrences but two patients had distant metastases. During the study period, eight patients underwent closure of their stoma, whilst the remaining three have had normal anastomotic assessments and will be closed in the future.

Conclusions:

This early series shows that implementation of taTME for resections beyond total mesorectal excision may be feasible and safe in a highly selected setting.

What does this paper add to the literature?

Whilst there is controversy surrounding the uptake and implementation of taTME, this early case series highlights the potential benefits of the utilization of taTME in specialized units in patients with locally advanced rectal cancer in whom resections beyond TME are necessary to achieve clear resection margins.

KEYWORDS

Total mesorectal excision, rectal cancer, extended resection, transanal TME, taTME

INTRODUCTION

Local recurrence rates have been a key quality indicator in the treatment of locally advanced rectal cancer. Better staging with magnetic resonance imaging (MRI), a multidisciplinary approach and combining neoadjuvant treatment with total mesorectal excision (TME) have yielded good oncologic results in these patients (1-3).

Although TME has become embedded as the gold standard procedure for locally advanced rectal cancer (LARC), surgical techniques have continued to evolve. These include radical resections beyond the TME plane for mesorectal fascia (MRF) or adjacent pelvic organ involvement (4,5). Due to their complexity and high morbidity rates, it has been advocated that such procedures are centralised to tertiary or quarternary referral centres(6). Specialist centres have reported favourable oncological outcomes after resections beyond TME for LARC. A recent large multicentric international collaboration reported a 56.4% 3-year overall survival for patients with LARC requiring resection beyond TME when an R0 resection was achieved (7-9).

Technology has also improved allowing surgeons to use minimally invasive approaches in selected patients requiring multivisceral resections for LARC. This has led to reduced intraoperative blood loss, shorter length of hospital stay, and reduced morbidity(10).

In addition to transabdominal minimally invasive approaches, transanal TME (taTME) has emerged from a fusion of concepts and technological developments: Heald's description of TME, Mark's transanal-transabdominal (TATA) dissection and the ´bottom-to-up´ approach, minimally invasive surgery and transanal access platforms such as Transanal Endoscopic Microsurgery (TEM) and ultimately Transanal Minimally invasive Surgery (TAMIS)(11-14). The rationale of utilising taTME in rectal cancer relates to a more controlled distal resection margin (DRM) and rectal transection, enhanced distal mesorectal dissection, and the ability to fashion a single-stapled anastomosis(15). Specifically, in LARC with MRF or adjacent organ involvement, taTME would facilitate the disconnection of the rectum distally, resection of adjacent pelvic structures, and control of the R1 risk-points during dissection.

This study aims to report the potential benefits of a transanal minimally invasive approach (taTME) in patients requiring resection beyond TME for LARC following the reporting standards of the IDEAL guidelines(16).

MATERIALS & METHODS

This was a retrospective review of patients undergoing radical resections beyond TME for LARC between January 2018 and December 2019. Data had been collected prospectively on separately maintained rectal cancer databases. Patients had undergone surgery in two centres: a public quaternary centre (Peter MacCallum Cancer Centre, Melbourne, Australia), and a private tertiary centre (Epworth Freemasons, Melbourne, Australia). Patients selected were those with a diagnosis of LARC, and MRF or adjacent organ involvement, where a taTME approach was part of the surgical strategy. Patients with non-curable metastatic rectal cancer were excluded.

All cases were routinely discussed in a multidisciplinary team meeting prior to treatment. All patients received neoadjuvant long-course chemoradiation (LCCRT), and were re-staged with a thorax-abdomen-pelvic computed-tomography (CT), positron-emission-tomography-CT (PET-CT) and pelvic MRI 4 to 5 weeks after neoadjuvant treatment. Surgery was scheduled beyond 8 weeks from LCCRT completion.

Data recollection

Patient demographic data, tumour characteristics, neoadjuvant and adjuvant treatment, operation details, perioperative results, histopathology and follow-up data were recorded.

Definitions

The clinical and histopathological staging was recorded according to the TNM classification (AJCC 8th Edition for Cancer Staging)(17). Clinical staging and re-staging were based on CT, PET-CT and MRI. Tumour distance from the anal verge (DAV) was defined clinically or by the pre-treatment MRI. Pre-operative tumour response to LCCRT was assessed in the re-staging MRI, using the MRI tumour regression grade (mrTRG)(18).

Pelvic side-wall lymph node metastases were defined as lymph nodes in the obturator fossa or internal iliac vessels territories, with a short axis > 7 mm in the pre-treatment MRI(19). When present, a pelvic side-wall lymph node dissection was indicated regardless of the nodal response to LCCRT.

Postoperative complications, readmissions and mortality were considered during the first 90 postoperative days, and complications were classified according to Clavien-Dindo(20). Ileus was defined as a functional obstruction of the gastrointestinal tract, marked by the absence of peristalsis, usually accompanied by abdominal bloating, and sometimes nausea and vomiting, requiring nasogastric tube insertion for more than 24 hours post-operatively. Anastomotic leak was defined as any clinical or radiological evidence of a defect of the intestinal wall at the anastomotic site, communicating the intra- and extra-luminal compartments.

The histopathological evaluation considered an R0 resection as a resection margin of > 1 mm. R1 was the presence of microscopic residual disease defined as a resection margin of ≤ 1 mm, whereas R2 resection was the presence of macroscopic residual disease.

Adjuvant chemotherapy consisted of capecitabine-oxaliplatin (CAPEOX) or folinic acid-fluorouracil-oxaliplatin (FOLFOX) administered over 6 months.

During follow-up, anastomotic integrity was assessed with a contrast enema study and flexible sigmoidoscopy. The presence of local or distant recurrence was confirmed in a multidisciplinary team meeting with consideration of clinical, radiological and endoscopic findings.

Procedure

Before surgery, patients had standard mechanical bowel preparation. The operating team was organised for a synchronous two-team procedure, which included two colorectal surgeons, two colorectal fellows and two scrub teams. SW and AH performed the taTME components of the operations. Both SW and AH are proctors for taTME, and conduct related courses. Furthermore, SW and AH have been involved in over 100 and 50 taTME cases since 2015, respectively.

General anaesthetic was given and prophylactic antibiotics were administered at induction. An indwelling urinary catheter was inserted, and the patient placed in the Lloyd-Davies position. All patients had sequential compression devices and ureteric stents placed before the operation. Low molecular weight heparin was given on induction, and throughout inpatient stay.

Transabdominal phase

The abdominal phase was performed via a robotic, laparoscopic or open approach on a case-by-case basis. This involved high ligation of the inferior mesenteric vessels, and full mobilisation of the splenic flexure in all cases. The ureters were identified, mobilised and protected when appropriate. Tumour resection involved dissection in the pelvis beyond the TME plane when needed, in continuous communication with the perineal team. When intraoperative radiotherapy (IORT) was necessary, high-dose-rate brachytherapy providing 10Gy to the R1 risk-point area was used(21). When a pelvic side-wall lymph node dissection was required, the ureter was mobilised and medialised to the vesico-ureteric junction, and dissection was carried out in a standardized fashion identifying the common iliac artery bifurcation, clearing the lymph nodes in the obturator fossa (preserving the obturator nerve), and the internal iliac system (Figure 1).

All patients received a defunctioning loop ileostomy and had a closed suction pelvic drain placed at the end of the procedure.

Perineal phase

The anus was everted with four 0 silk sutures placed in four quadrants, and a Lonestar Retractor (Lonestar, Cooper Surgical, Trumbull, CT, USA) used to retract the anoderm. The anal canal was then washed with cetrimide. The GelPoint Path (Applied Medical, Rancho Santa Margarita, CA, USA) was then inserted, and a 1-0 prolene suture with a 26-mm rounded needle used to create a purse-string to close the rectum, distal to the lesion. The platform cap with three ports was then placed, and a pneumorectum established with an AirSeal® System (Conmed, Connecticut, USA) at a flow rate of five litres per minute, and a pressure of 5 mmHg. A 5 mm SILS ™ Hook diathermy (Covidien, Dublin, Ireland) with articulation ability is used to perform a full-thickness circumferential rectotomy under a 0-degree laparoscope vision. The GelPoint Path was then removed and the purse string reinforced with 1-0 prolene, inverting the mucosa. A cetrimide wash was again performed, the GelPoint Path repositioned, the camera switched to a 30-degree laparoscope, and pressure from the AirSeal was increased to 12 mmHg. ´Down-to-up´ dissection was carried out through the TME plane, until planes beyond TME (presacral, side-wall or Denonvilliers´ fascia, seminal vesicles, vagina, etc.) needed to be dissected in order to achieve an R0 resection, in a combined transabdominal and transanal effort. Dissection was undertaken using diathermy and advanced energy devices.

Anastomosis

The anastomosis was handsewn or stapled depending on the height of the remaining rectal cuff. Handsewn anastomoses were fashioned using interrupted 3-0 Vicryl sutures. Stapled anastomoses were performed using a double purse-string techniquewith a 33-mm haemorrhoidal stapler (DST Series™ Technology - Covidien, Dublin, Ireland) (22),. An end-to-end or a 6 cm colonic-pouch-anal anastomosis was fashioned according to the surgeons´ preference. A rectal tube was usually left in situ for 24 hours.

Postoperatively, an ERAS (Enhanced Recovery After Surgery) protocol was followed.

Statistical analysis

All characteristics were summarised using descriptive statistics, including counts and frequencies for categorical variables, and median and range for continuous variables. All statistical analyses were performed using Microsoft Excel 2010.

Ethics

Patients were consented specifically for this approach. Institutional Review Board ethics approval were obtained from both sites for quality assurance. Reference numbers are PMCC2020-63744 and EH2020-559.

RESULTS

Demographic data, tumour characteristics and pre-treatment details

During the study period 78 patients had extended pelvic resections of which 51 were for LARC. Inclusion criteria were met by 11 (6 males; median age :52 (42-62) years; median BMI 22.9 (21.5-26.1) kg/m$^{2)}$. All had rectal adenocarcinomas, and the median DAV was 7 (7-9) cm. Ten patients were clinically stage II or III, and one had stage IV disease (patient 8). Median time from completion of LCCRT to surgery was 11 (11-14) weeks (Table 1). Patient 8 refused surgery after LCCRT, represented with a single lung metastasis and received systemic chemotherapy, before undergoing a wedge resection via video-assisted thoracoscopy. Histopathological analysis of this specimen revealed a positive resection margin (R1 resection). He had no metastatic disease in his restaging imaging three months after lung resection and the multidisciplinary team decision offered the patient further radical treatment.

Perioperative and histopathological outcomes

The transabdominal approach was open in five cases, robotic in four and laparoscopic in two. All patients required resection of adjacent structures: presacral fascia or periosteum (n=5), uterus and posterior vaginectomy (n=3), ureteric resections (n=3) Denonvillier´s fascia and seminal vesicles (n=2), internal iliac vessels resection (n=2), partial vaginectomy (n=1), sacral nerve roots and piriformis muscle resection (n=1), and anterior table of the sacrum (n=1). Four patients required pelvic side-wall lymph node dissections. Four patients had IORT.

The transanal approach was used to disconnect the rectum distally, resect adjacent organs, and control the R1 risk-point. Specific components of the taTME approach for each case are detailed in Table 2.

There was one reactive conversion due to a proximal inferior mesenteric artery injury, during dissection in a transabdominal robotic phase. This was controlled with pressure using a laparoscopic grasper through the assistant port, allowing the team to perform a controlled laparotomy.

The median operative time and blood loss were 410 (385-495) min and 300 (200-750) ml, respectively. The median length of stay was 7 (7-16) days.

Four patients had postoperative complications of which three were Clavien-Dindo ≥ III (one mechanical bowel obstruction requiring return to theatre, a pelvic collection requiring CT-drainage, and a urine sepsis requiring antibiotics and change of ureteric stents). The pelvic collection was associated with a possible thermal injury in the descending colon - a seven mm defect was visualized three to four cm above the anastomosis during an endoscopic evaluation and washout (patient 7). After carrying out endoscopic washouts and antibiotic treatment this eventually closed. There were no anastomotic complications.

Perioperative outcomes are summarised in Table 2. There was no mortality in this series. All patients had clear CRM and DRM. An R0 resection was achieved in ten patients (Table 3). Although patient 8 had a 0.6 mm posterior CRM in the histopathological analysis, an anterior table sacrectomy (not *en bloc*) had been performed at this level with local IORT. There were no cancer cells visualised in the bone specimen in the histopathological review.

Adjuvant treatment and follow-up

Four patients did not receive adjuvant treatment; two of them due to postoperative complications, one due to total upfront chemotherapy in the context of a stage IV disease and another one refused to have adjuvant chemotherapy (Table 4).

During a median follow-up of 11 (8.6-16) months, no patients had local recurrences although two patients developed distant metastases. Eight patients had their stomas reversed, whilst the remainng three went on to have normal contrast enemas and endoscopic assessments, and have been waitlisted for stoma closure (Table 4). Delays experienced in stoma closures were largely due to the COVID-19 pandemic .

DISCUSSION

Our preliminary results show that the application of taTME in selected patients with LARC requiring resection beyond TME is feasible by utilising ´false planes´ in otherwise complex oncological scenarios. The current study shows that good short-term outcomes are possible when there is an uptake of surgical advances by specialist units, provided oncological principles and multidisciplinary care are followed.

The rationale behind utilising a taTME approach arises predominantly from making sure the R1 risk-point is visualised and controlled. This concept has been previously highlighted by the authors(23). In this series, all patients received a restorative procedure: taTME facilitated this by disconnecting the rectum distally, therefore ensuring the distal pelvic dissection was completed before dealing with the R1 risk-point or significant risk of bleeding (especially when performing pelvic side-wall dissections or resections, or bony resections).

There are three scenarios where taTME can be used for the oncological and reconstructive purposes of patients with LARC:

1. Postero-lateral advanced rectal cancers; with or without major vascular resection (Figure 2)
2. Anterior advanced rectal cancers in males; allowing for selective removal of seminal vesicles (Figure 3)
3. Anterior advanced rectal cancers in females; requiring *en bloc* vaginectomy, and or hysterectomy (Figure 4)

The first scenario is where postero-lateral structures are involved. The fundamental role of a taTME approach here is to disconnect for reconstruction, and strip both the presacral fascia off the bone and the pelvic side-wall endopelvic fascia. This is ensured by following ´false planes´. The approach also allows the team to perform IORT. Our group recently reported the first case where IORT was provided via a transanal approach (24).

In the second scenario, the urogenital structures, specifically the seminal vesicles or prostate, are at risk or invaded. The transanal approach ensures the caudal part of Denonvilliers´ fascia is transected. Then, a partial prostatectomy or seminal vesicles resection can be performed if required. This is easier than exclusively undertaking a top-down approach, given that in the setting of a narrow pelvis or bulky tumour, resecting the rectum plus *en bloc* seminal vesicles or prostate in a controlled manner can be challenging (25).

The third scenario is where a bulky tumour abuts or invades the cervix or vagina. Again, utilising taTME helps to obtain a clear demarcation of the inferior border of invasion in the genital structures (R1 risk-point). This allows for a synchronous transanal posterior vaginectomy, and abdominal hysterectomy, if required (23,26).

Current literature would support taTME uptake and utilization when performed by trained specialist surgeons in high-volume centres. Systematic reviews and meta-analyses based on comparative retrospective data have demonstrated lower rates of CRM positivity in the taTME group compared to pure laparoscopic cohorts (27,28). In a Dutch study based on follow-up data from 159 patients undergoing taTME for rectal cancer in two high-volume referral centres, the reported 5-year local recurrence rate was 4%, and the median time to local recurrence was 19.2 months (29). The authors concluded taTME was associated with favourable oncologic outcomes when performed by experienced surgeons in tertiary referral centres. In another multicentric study, including 767 patients from 6 tertiary referral centres across Europe and the USA, the cumulative 2-year local recurrence rate was 3% with no patient developing a multifocal pattern of local recurrence. Similarly, the authors concluded that taTME was associated with reasonable intermediate-term oncologic results in this complex cohort of patients (30). Aditionally, other authors have shown, after adjusting for confounders, that high anastomotic leak rates seen in taTME patients are due to anastomoses in the lowest part of the rectum or the anus. Anastomotic leak rates in low rectal anastomoses remain high, regardless of the operative approach (31).

Recent Norwegian data have raised concerns related to recurrence rates, patterns of recurrence, and anastomotic leak rates with taTME. The estimated local recurrence rate at 2.4 years was 11.6%. Fifty percent were multifocal, with or without distant metastasis. It is worth noting the low uptake of preoperative radiation in the taTME group compared with the national cohort (21% vs. 39%; P=0,001). There was also a high rate of pathologically positive or submillimetre margin rate (12.7%) in the taTME group, greater than that reported in other specialist centres (32). Other groups have also reported a multifocal local-recurrence pattern, questioning the quality of surgery rather than the technique itself (30). Part of the problem may be due to inappropriate patient selection or relate to surgery being performed during the learning curve. Recent data from Australia and New Zealand have also raised concerns about high unadjusted leak rates associated with taTME (33). All of these concerns have led the Association of Coloproctology of Great Britain and Ireland to recommend a pause in carrying out taTME until further long-term follow-up information validates its utilisation (34).

The understanding of the potential limitations and risks associated with taTME uptake has led to the development of training models and structured training programs with the aim of preventing poor oncologic outcomes and iatrogenic injuries during the learning curve (35–37). Even though some accept that taTME uptake is safe amongst specialised units under strict criteria, further oncologic follow-up data will be needed to validate its utilisation.

The limitations of this study include the small number of cases analysed, the heterogeneous group of oncologic scenarios, the limited oncologic follow-up and the lack of functional information in the scenario of restorative procedures albeit extended pelvic resections. However, we believe this is the first publication to detail the use of taTME for such complex patients. We acknowledge that this study does not report long-term oncological outcomes for taTME, but it does demonstrate that it can be safely offered in complex oncological scenarios, provided the team is adequately trained in open and minimally invasive complex pelvic surgery. The authors do not advocate these approaches should be carried out by all taTME competent surgeons, but by those teams who are familiar with the set up and surgical anatomy of beyond standard TME planes and have experience in such operations. A broader experience is required to validate the short-term and oncologic outcomes of these approaches. Multicentric international collaborations such as the PelvEx consortium could help migrate from the proof of concept and development stages, to learning and assessment phases, refining the potential role and indications of more advanced applications of taTME(16).

Whilst there is already evidence to suggest that laparoscopic and robotic surgery can be safely applied to highly-selected patients requiring pelvic exenterations, technology continues to evolve (10). Therefore, patients with challenging LARC will continue to be offered novel minimally invasive techniques ensuring an R0 resection is achieved, with restoration of intestinal continuity to remain an option in such scenarios.

CONCLUSION

This early series shows that implementation of taTME for resections beyond total mesorectal excision for LARC may be feasible and safe in a highly selected setting. Further studies and oncological data are required to validate this approach for LARC.

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None

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TABLES AND FIGURES

Figure 1. Critical view of a pelvic side-wall lymph node dissection showing clearance of a) common and external iliac vessels territories, b) obturator fossa with the obturator nerve preserved, and c) internal iliac vessels territories. Ureter is medialised and looped with a blue vascular tape

Figure 2. Postero-lateral advanced rectal cancer pattern. a) Sagittal view of the restaging MRI of patient 8 showing periosteum invasion at S2 level (red arrow); b) intraoperative picture showing ULAR with presacral fascia en bloc + S2 anterior table sacrectomy as further margin before IORT (blue arrow)

Figure 3. Anterior advanced rectal cancer in male pattern. a) Restaging MRI of patient 10 showing persistent left seminal vesicle involvement (red arrow); b) intraoperative picture showing the resection bed of the left seminal vesicle (blue arrow).

Figure 4. Anterior advanced rectal cancer in female pattern. a) Restaging MRI of patient 4 showing persistent invasion of posterior vaginal wall (red arrow); b & c) transanal and transabdominal views showing distal vaginal wall breakthrough via the perineal approach

Table 1. Patient demographic data and tumour characteristics

Table 2. Procedure details and perioperative outcomes

Table 3. Histopathological data

Table 4. Adjuvant therapy and follow-up data

Table 1. Patient demographic data and tumour characteristics

P	*Procedure*	*Transanal approach*	*Anastomosis*	*Operative time (min)*	*Blood loss (ml)*	*F… c… (…*

							pre-sacral fascia at S2/3 level	deposit invading
2	44	F	20	III	7	III	cT4bN2; invasion of posterior cervix	ymrT3N1; TRG 3
3	52	F	21	III	6	III	cT4bN2; invasion of posterior cervix and vaginal wall	ymrT4bN0; TRG invasion
4	60	F	21.9	II	4	III	cT3bN2; threatened (0.5 mm) right anterior CRM (cervix/posterior vagina)	ymrT3bN2; TRG threatened CRM side-wall lymph
5	35	M	22	I	10	II	cT4bN0; invasion of right seminal vesicle	ymrT4bN0; TRG invasion of right
6	31	F	26.2	I	6	III	cT4bN1a; invasion of posterior vagina below cervix, right pelvic sidewall lymph node	ymrT4bN1a; TR posterior vaginal right pelvic side-
7	64	M	26	I	14	III	cT4bN2; invasion of presacral fascia at S2/3 level; bilateral pelvic side-wall lymph nodes	ymrT4bN2; TRG presacral invasio pelvic side-wall l
8	63	M	22.9	III	8	IV (resected lung metastasis)	cT3cN1	ymrT4bN0; TRG invasion at S2 le
9	39	M	29.5	I	12	III	cT3N1a; tumor deposit invading presacral fascia at S1 level; left pelvic side-wall lymph node	ymrT3cN1a; TR deposit invasion and left pelvic si
10	44	M	24.9	I	7	II	cT4bN0; invasion of left seminal vesicle	ymrT4bN0; TRG seminal vesicle i
11	69	M	30.4	II	7	III	cT4bN2; tumor deposit invading internal iliac vessel branches and contacting left S2-3 nerve roots and piriformis muscle; left pelvic side-wall lymph nodes	ymrT4bN2; TRG deposit invading pelvic side-wall l

P = patient; BMI = body mass index; ASA = American Society of Anaesthesiologist classification; cStage = clinical stage; MRI = magnetic resonance imaging; F = female; M = male; TRG = tumor regression grade; CRM = circumferential resection margin; n/a = not applicable

1	Laparoscopic ULAR + left ureterolysis + *en bloc* presacral fascia + IORT + left pelvic side wall LND	Disconnect, presacral stripping, deliver IORT transanally	Stapled, colonic pouch	390	200	N
2	Robotic ULAR + *en bloc* hysterectomy, bilateral salpingo-oophorectomy and posterior vaginectomy	Disconnect, posterior vaginectomy	Stapled, colonic pouch	410	100	N
3	Robotic ULAR + *en bloc* hysterectomy, bilateral salpingo-oophorectomy and posterior vaginectomy	Disconnect, posterior vaginectomy	Stapled, colonic pouch	430	100	S c
4	Robotic ULAR + *en bloc* hysterectomy, bilateral salpingo-oophorectomy and posterior vaginectomy + left pelvic sidewall LND	Disconnect, posterior vaginectomy	Handsewn, end-to-end	480	500	I
5	Laparoscopic ULAR + *en bloc* right ureter, bilateral seminal vesicles, bladder cuff, right pelvic side-wall dissection, primary uretero-vesicle anastomosis (via lower midline incision)	Disconnect, Denonvilliers´ fascia and seminal vesicles	Stapled, end-to-end	380	300	U r r
6	Robotic (converted) ULAR + *en bloc* partial posterior vaginectomy + right pelvic sidewall LND	Disconnect, partial posterior vaginectomy	Stapled, colonic pouch	240	400	N
7	Open ULAR + *en bloc* right ureter, appendix, periosteum of S1-S3 and bilateral pelvic sidewall LND, IORT to the sacrum with primary ureteric reimplantation	Disconnect, presacral fascia resection and periosteum stripping	Stapled, end-to-end	510	1500	P
8	Open ULAR + *en bloc* presacral fascia and periosteum of L5/S1 + anterior table S2 sacrectomy (not *en bloc*) + IORT	Disconnect, presacral fascia resection	Stapled, colonic pouch	660	2000	N
9	Open ULAR + *en bloc* left ureter, presacral fascia S1-2 level and anterior division of left internal iliac artery + IORT + Boari flap and ureteric reimplantation	Disconnect, presacral fascia and left endopelvic fascia resection	Stapled, colonic pouch	510	300	U r
10	Open ULAR + *en bloc* left vas deferens and seminal vesicle, Denonvilliers´ fascia and partial prostatectomy	Disconnect, Denonvilliers´ fascia and left seminal vesicle resection	Stapled, end-to-end	300	200	N
11	Open ULAR + *en bloc* presacral fascia, left internal iliac artery and vein, left S2/3 nerve roots and partial piriformis muscle resection	Disconnect, presacral fascia and left endopelvic fascia resection	Stapled, colonic pouch	390	1000	U r

Table 2. Procedure details and perioperative outcomes

P = patient; LOS = length of stay; ULAR = ultra-low anterior resection; IORT = intraoperative radiotherapy; LND = lymph node dissection

Table 3. Histopathological data

P	*TNM*	*Resection status*	*CRM (mm)*	*DRM (mm)*	*TRG*	*Mesorectal LN*	*Side-wall LN*
1	ypT3N2bMx	R0	1.5	53	2	2/14	*en bloc*
2	ypT3N0Mx	R0	8	15	1	0/17	n/a
3	ypT3N0Mx	R0	> 10	45	1	0/31	n/a
4	ypT3N1bMx	R0	> 10	6	3	1/22	1/11
5	ypT4bN1cMx	R0	6	80	1	0/17	n/a
6	ypT3N1aMx	R0	> 10	30	1	0/8	1/3
7	ypT3N0Mx	R0	3	61	3	0/14	0/15
8	ypT3N0Mx	R1*	0.6	14	n/a	0/13	n/a
9	ypT3N1cMx	R0	2	80	2	0/20	*en bloc*

10	ypT3N1aMx	R0	10	17	2	1/14	n/a
11	ypT3N1cMx	R0	10	10	2	0/11	*en bloc*

P = patient; TNM (AJCC 8th Edition); CRM = circumferential resection margin; DRM = distal resection margin; TRG = tumour regression grade (as per Ryan et al. classification); LN = lymph nodes

* Before an additional margin was taken by performing an anterior table S2 sacrectomy plus intraoperative radiotherapy to the area. The histopathological analysis of the bone specimen didn´t reveal any cancer cells

Table 4. Adjuvant therapy and follow-up data

P	*Completed adjuvant therapy*	*Follow-up (months)*	*LR*	*DR*	*Stoma closure*
1	Yes	18	No	Lungs (12 months)	Yes
2	Yes	25	No	Liver, lungs, bones (12 months)	Yes
3	Yes	12	No	No	Yes
4	Yes	8	No	No	Planned
5	Yes	21	No	No	Yes
6	Yes	15	No	No	Yes
7	No*	9	No	No	Planned
8	No**	11	No	No	Yes
9	No*	11	No	No	Yes
10	No***	8	No	No	Yes
11	Yes	9	No	No	Planned

P = patient; LR = local recurrence; DR = distal recurrence (diagnosis in months from surgery)

* Due to complications

** Had chemotherapy upfront

*** Refused adjuvant treatment

Table 1. Patient demographic data and tumour characteristics

P	*Age*	*Sex*	*BMI*	*ASA*	*DAV (cm)*	*cStage*	*Pre-treatment MRI*	*Post-treatment MRI*	*Weeks to surgery*
1	53	F	16.5	I	7	III	cT4aN1c; tumor deposit invading pre-sacral fascia at S2/3 level	ymrT3cN1c; TRG 3; persistent deposit invading presacral fascia	10
2	44	F	20	III	7	III	cT4bN2; invasion of posterior cervix	ymrT3N1; TRG 3	11
3	52	F	21	III	6	III	cT4bN2; invasion of posterior cervix and vaginal wall	ymrT4bN0; TRG 2; persistent CRM invasion	12
4	60	F	21.9	II	4	III	cT3bN2; threatened (0.5 mm) right anterior CRM (cervix/posterior vagina)	ymrT3bN2; TRG 2-3; persistently threatened CRM and positive left side-wall lymph nodes	9
5	35	M	22	I	10	II	cT4bN0; invasion of right seminal vesicle	ymrT4bN0; TRG 3; persistent invasion of right seminal vesicle	11
6	31	F	26.2	I	6	III	cT4bN1a; invasion of posterior vagina below cervix, right pelvic sidewall lymph node	ymrT4bN1a; TRG 2-3; persistent posterior vaginal wall invasion and right pelvic side-wall lymph node	10
7	64	M	26	I	14	III	cT4bN2; invasion of presacral fascia at S2/3 level; bilateral pelvic side-wall lymph nodes	ymrT4bN2; TRG 3-4; persistent presacral invasion and bilateral pelvic side-wall lymph nodes	11
8	63	M	22.9	III	8	IV (resected lung metastasis)	cT3cN1	ymrT4bN0; TRG n/a; periosteum invasion at S2 level	130
9	39	M	29.5	I	12	III	cT3N1a; tumor deposit invading presacral fascia at S1 level; left pelvic side-wall lymph node	ymrT3cN1a; TRG 4-5; persistent deposit invasion of presacral fascia and left pelvic side-wall lymph node	16

10	44	M	24.9	I	7	II	cT4bN0; invasion of left seminal vesicle	ymrT4bN0; TRG 3; persistent left seminal vesicle invasion	12
11	69	M	30.4	II	7	III	cT4bN2; tumor deposit invading internal iliac vessel branches and contacting left S2-3 nerve roots and piriformis muscle; left pelvic side-wall lymph nodes	ymrT4bN2; TRG 4; persistent deposit invading through CRM and pelvic side-wall lymph nodes	16

P = patient; BMI = body mass index; ASA = American Society of Anaesthesiologist classification; cStage = clinical stage; MRI = magnetic resonance imaging; F = female; M = male; TRG = tumor regression grade; CRM = circumferential resection margin; n/a = not applicable

Table 2. Procedure details and perioperative outcomes

P	*Procedure*	*Transanal approach*	*Anastomosis*	*Operative time (min)*	*Blood loss (ml)*	*Postoperative complications (Clavien)*	*LOS*
1	Laparoscopic ULAR + left ureterolysis + *en bloc* presacral fascia + IORT + left pelvic side wall LND	Disconnect, presacral stripping, deliver IORT transanally	Stapled, colonic pouch	390	200	No	7
2	Robotic ULAR + *en bloc* hysterectomy, bilateral salpingo-oophorectomy and posterior vaginectomy	Disconnect, posterior vaginectomy	Stapled, colonic pouch	410	100	No	4
3	Robotic ULAR + *en bloc* hysterectomy, bilateral salpingo-oophorectomy and posterior vaginectomy	Disconnect, posterior vaginectomy	Stapled, colonic pouch	430	100	Small bowel obstruction (III)	14
4	Robotic ULAR + *en bloc* hysterectomy, bilateral salpingo-oophorectomy and posterior vaginectomy + left pelvic sidewall LND	Disconnect, posterior vaginectomy	Handsewn, end-to-end	480	500	Ileus (II)	23
5	Laparoscopic ULAR + *en bloc* right ureter, bilateral seminal vesicles, bladder cuff, right pelvic side-wall dissection, primary uretero-vesicle anastomosis (via lower midline incision)	Disconnect, Denonvilliers´ fascia and seminal vesicles	Stapled, end-to-end	380	300	Urinary sepsis (III), recurrent readmissions	7
6	Robotic (converted) ULAR + *en bloc* partial posterior vaginectomy + right pelvic sidewall LND	Disconnect, partial posterior vaginectomy	Stapled, colonic pouch	240	400	No	5
7	Open ULAR + *en bloc* right ureter, appendix, periosteum of S1-S3 and bilateral pelvic sidewall LND, IORT to the sacrum with primary ureteric reimplantation	Disconnect, presacral fascia resection and periosteum stripping	Stapled, end-to-end	510	1500	Pelvic collection (III)	17
8	Open ULAR + *en bloc* presacral fascia and periosteum of L5/S1 + anterior table S2 sacrectomy (not *en bloc*) + IORT	Disconnect, presacral fascia resection	Stapled, colonic pouch	660	2000	No	7
9	Open ULAR + *en bloc* left ureter, presacral fascia S1-2 level and anterior division of left internal iliac artery + IORT + Boari flap and ureteric reimplantation	Disconnect, presacral fascia and left endopelvic fascia resection	Stapled, colonic pouch	510	300	Urinary sepsis (II), readmission	21

10	Open ULAR + *en bloc* left vas deferens and seminal vesicle, Denonvilliers´ fascia and partial prostatectomy	Disconnect, Denonvilliers´ fascia and left seminal vesicle resection	Stapled, end-to-end	300	200	No	10
11	Open ULAR + *en bloc* presacral fascia, left internal iliac artery and vein, left S2/3 nerve roots and partial piriformis muscle resection	Disconnect, presacral fascia and left endopelvic fascia resection	Stapled, colonic pouch	390	1000	Urinary sepsis (II), readmission	7

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9	ypT3N1cMx	R0	2	80	2	0/20	*en bloc*
10	ypT3N1aMx	R0	10	17	2	1/14	n/a
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9	No*	11	No	No	Yes
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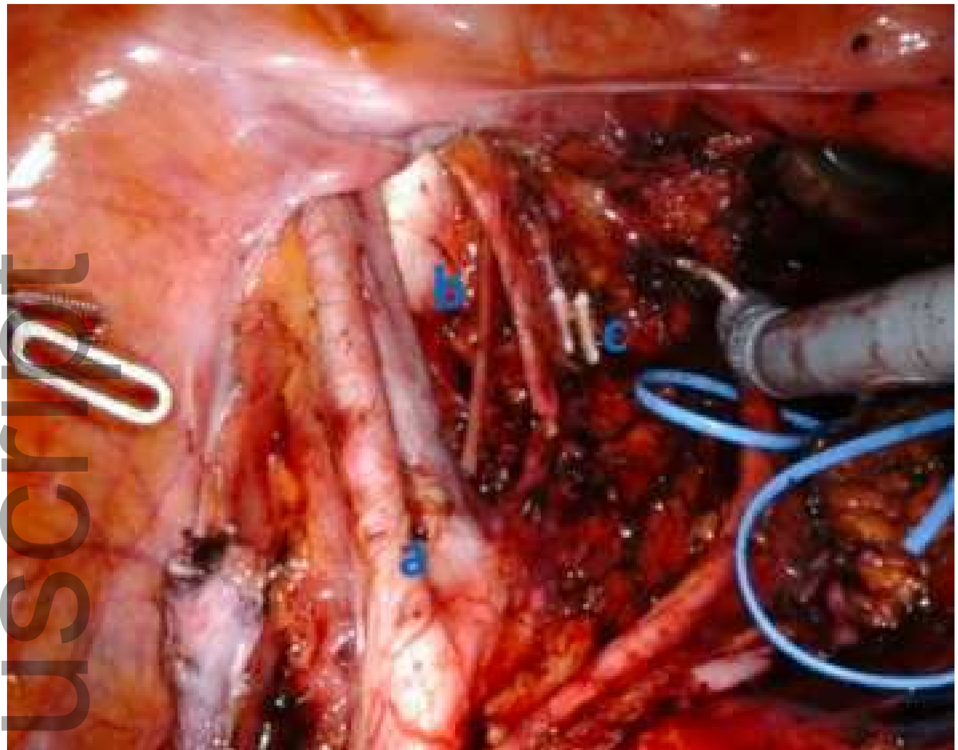

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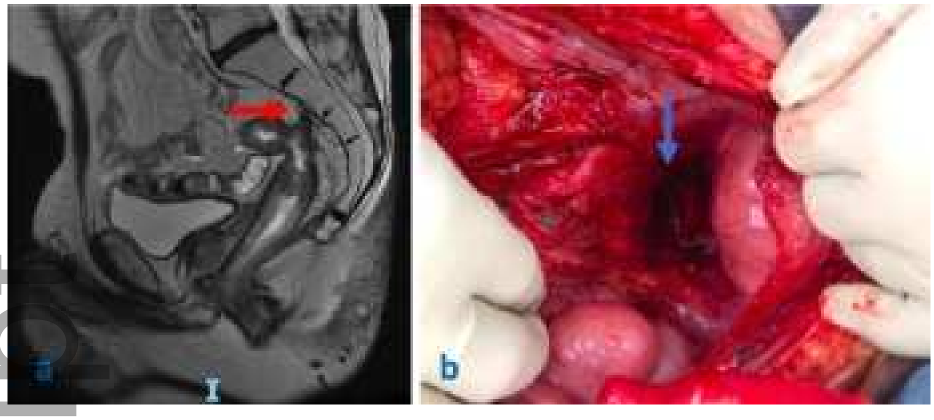

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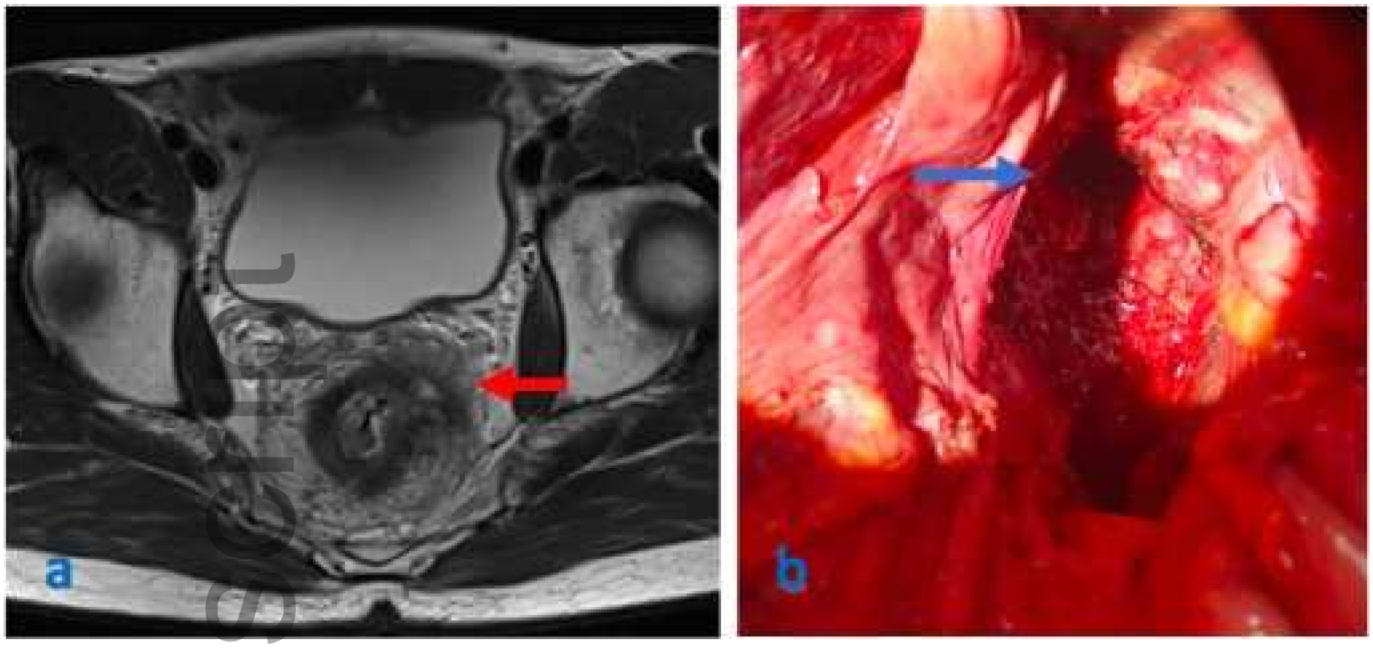

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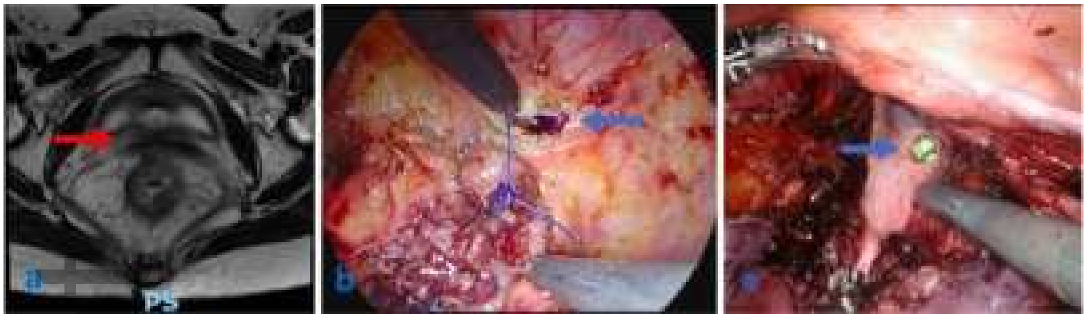

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