NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of transanal total mesorectal excision for rectal cancer

Rectal cancer affects the end part of the bowel (rectum). In this procedure, the whole rectum is removed (total mesorectal excision). This is done using instruments introduced through the anus (transanal) and by keyhole surgery through the abdomen. The aim is to remove all the cancer.

Contents

Abbreviations

Word or phrase	Abbreviation
Confidence interval	CI
Circumferential resection margin	CRM
Distal resection margin	DRM
European Organisation for Research and Treatment of Cancer	EORTC
Hazard ratio	HR
Interquartile range	IQR
International prostate syndrome score	IPSS
Low anterior resection syndrome	LARS
Mean difference	MD
Norwegian colorectal cancer registry	NCCR
Norwegian registry of gastrointestinal surgery	NoRGast
Odds ratio	OR
Transanal total mesorectal excision	TaTME
Total mesorectal excision	TME
Tumour Node Metastasis	TNM
Quality-of-life questionnaire	QLQ
Relative risk	RR

Introduction

The National Institute for Health and Care Excellence (NICE) prepared this interventional procedure overview to help members of the interventional procedures advisory committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and professional opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in March 2021 and updated in October 2021.

Procedure name

- Transanal total mesorectal excision for rectal cancer

Professional societies

- Association of Coloproctology of Great Britain and Ireland
- BASO – The Association for Cancer Surgery
- Association of Surgeons of Great Britain and Ireland.

Description of the procedure

Indications and current treatment

The incidence of rectal cancer rises sharply with age. Symptoms include rectal bleeding and change in bowel habit, although the early stages may be asymptomatic.

The management of rectal cancer is described in the NICE guideline on colorectal cancer. The main treatment is surgery. It involves resecting the affected part of the rectum, with anus preservation or, when anus preservation is not technically possible, colostomy formation. Adjunctive radiotherapy and chemotherapy may also be used to reduce the risk of local recurrence and prevent metastatic disease.

What the procedure involves

The aim of TaTME is to improve the clinical outcome of rectal resection, and to reduce length of hospital stay and morbidity after surgery. It may enable proctectomy (removal of all or part of the rectum) that would be difficult by an open or laparoscopic approach. This could be in people with a narrow pelvis or high body mass index, or where the position of the tumour is low in the rectum.

Before surgery, the patient has bowel preparation and prophylactic antibiotics. Using general anaesthesia, and with the patient in the lithotomy position, standard abdominal laparoscopic mobilisation of the left colon and upper rectum is done. After inserting an operating platform into the anus, the lower rectum including the total mesorectum is mobilised. At the start of the transanal part of the procedure, a purse-string suture is put in to close the rectal lumen. This is

followed by a full thickness rectotomy. After identifying the TME plane, the dissection progresses proximally until it connects with the dissection from above. The specimen can be removed through the transanal platform or, if the tumour is large, through the abdomen using a small incision. Anastomosis to connect the colon and the anus can be done using sutures (hand-sewn technique) or staples, and a temporary ileostomy is usually created. When anastomosis is not possible, a permanent stoma is created.

Outcome measures

Colorectal cancer classification

The TNM classification system for malignant tumours is used to describe the stage of a cancer. 'T' describes the size and location of the primary tumour, including whether it has invaded surrounding tissue. 'N' describes the extent of cancer spread to local or regional lymph nodes. 'M' describes the degree of distant metastasis. The following classification applies to colorectal cancer:

- T0: there is no evidence of colorectal cancer
- T1: the tumour has grown into the submucosa
- T2: the tumour has grown into the muscularis propria
- T3: the tumour has grown through the muscularis propria into pericolorectal tissues
- T4a: the tumour penetrates the surface of the visceral peritoneum, meaning that it has grown through all layers of the colon
- T4b: the tumour has grown into or has attached to other organs or structures.

LARS score

The LARS score is a self-reported questionnaire used to measure bowel dysfunction after low anterior resection for rectal cancer. It contains 5 questions on incontinence to flatus or liquid stools, frequency of bowel motions, stool clustering and urgency. Overall scores are classified into 3 groups corresponding to the severity of LARS: no LARS (0 to 20), minor LARS (21 to 29), and major LARS (30 to 42).

EORTC QLQ (QLQ-C30 and QLQ-C29)

The QLQ-C30 questionnaire measures the quality of life of patients with cancer. It consists of 30 questions with 5 functional aspects (physical, role, emotional, cognitive and social), 8 symptoms (fatigue, nausea, pain, dyspnoea, loss of appetite, insomnia, constipation, and diarrhoea), financial strain and global health status. The complementary QLQ-29 assesses quality of life in patients with

colorectal cancer, with 29 questions in 4 scales (body image, urinary frequency, blood and mucus in stool, and stool frequency).

Efficacy summary

Recurrence

In a systematic review of 638 patients, the local recurrence rate was 2.1% in patients who had TaTME and 3.2% in patients who had laparoscopic TME (OR 0.78, 95% CI 0.22 to 2.79, p=0.71, I^2=0%; 6 studies). The distant metastasis rates were 7.1% for TaTME and 13.3% for laparoscopic TME (OR 0.53, 95% CI 0.19 to 1.47, p=0.23, I^2=0%; 3 studies; Alimova 2021).

In a cohort study of 157 patients, local recurrence was reported in 8% (12/152) after a median follow up of 19.5 months. Of the 12 patients with local recurrences, 4 had R1 resections and 8 had R0 resections. The recurrences were described as multifocal in 6 patients and extensive in 2; 1 was in the staple line and 1 presacral. The recurrences in the other 2 patients were described as probably being derived from the pelvic lymph nodes. Only 1 patient diagnosed with local recurrence had preoperative chemoradiotherapy. All recurrences in the TaTME cohort occurred within 2 years of surgery, with a median of 9·5 months (range 2 to 23). The univariable hazard ratio for local recurrence after TaTME compared with a national cohort of patients who had open or laparoscopic rectal resection procedures for stage 1 to 3 rectal cancer was 5·70 (95% CI 2·70 to 12·06, p<0·001; Wasmuth 2020).

In a non-randomised comparative study of 710 patients, the proportion of patients with a locoregional recurrence was 4% with TaTME (95% CI 1.1 to 6.1) and 10% with laparoscopic TME (95% CI 6.5 to 12.7; HR=0.4, 95% CI 0.23 to 0.69, p=0.001; de Lacy 2020).

In a cohort study of 608 patients, the local recurrence rate was 4% (22/608). The median time to local recurrence was 13 months. The systemic recurrence rate was 9% (57/608; Caycedo-Marulanda 2021).

In a cohort study of 624 patients, the local recurrence rate was 5% (30/624) after a median interval of 17 months from index surgery. A multifocal pattern was seen in 6 of the local recurrences. Kaplan–Meier survival analysis showed an estimated local recurrence rate in the total study population of 5% at 2 years and 7% at 3 years. Comparative analyses of 3 predefined cohorts showed a 3-year local recurrence rate of 14% in the initial implementation, 5% during continued adoption and 6% with prolonged experience cohorts (p=0.036). Adjusted Cox regression analysis to correct for case mix projected the 3-year local recurrence rate to be 10%, 3% and 3% for the 3 cohorts respectively. Both the continued adoption cohort (HR 0.290, 95% CI 0.108 to 0.780, p=0.014) and prolonged experience cohort (HR 0.318, 95% CI 0.127 to 0.795, p=0.014) had a statistically

significant lower hazard of developing a local recurrence compared with the initial implementation cohort (Van Oostendorp 2021).

In a cohort study of 767 patients, local recurrence was reported in 3% (24/767) after a median follow up of 25.5 months and the median time to local recurrence was 13.5 months. The actuarial rate of local recurrence was 3% at 2 years and 4% at 3 years (Roodbeen 2020).

In a randomised controlled trial of 100 patients, the 5-year recurrence rate was 16% with TaTME and 25% with laparoscopic TME (p=0.129) and the mean time to recurrence was 21 months with TaTME and 10 months with laparoscopic TME. The 5-year local recurrence rate was 3% in the TaTME group and 5% in the laparoscopic TME group (p=0.300; Denost 2018).

Survival

In the systematic review of 638 patients, 2-year overall survival and 2-year disease-free survival were reported in 3 studies. They were similar for TaTME (RR 1.04, 95% CI 0.97 to 1.11, p=0.25, I^2=27%) and laparoscopic TME (1.01, 95% CI 0.92 to 1.11, p=0.86, I^2=0%; Alimova 2021).

In the non-randomised comparative study of 710 patients, disease-free survival rates at 3 years were 74% with TaTME and 69% with laparoscopic TME (HR=0.81, 95% CI 0.65 to 1.02, p=0.078). Overall survival rates at 3 years were 87% with TaTME and 82% with laparoscopic TME (HR=0.74, 95% CI 0.53 to 1.03, p=0.076; de Lacy 2020).

In the cohort study of 608 patients, probability of disease-free survival was 91% at 24 months, 88% at 36 months and 85% at 48 months (Caycedo-Marulanda 2021).

In the cohort study of 767 patients, actuarial disease-free survival was 82% at 2 years and 78% at 3 years. Actuarial overall survival was 95% at 2 years and 93% at 3 years (Roodbeen 2020).

In the randomised controlled trial of 100 patients, 5-year disease-free survival was 74% with TaTME and 72% with laparoscopic TME (p=0.351). Overall survival at 5 years was 87% with TaTME and 74% with laparoscopic TME (p=0.135; Denost 2018).

R0 resection

In a systematic review of 2,048 patients, the rate of R0 resection was 96% with TaTME and 93% with laparoscopic TME (OR 1.67, 95% CI 1.12 to 2.50, p=0.01; I^2=0%, 17 studies; Hajibandeh 2020).

In the cohort study of 767 patients, composite optimal pathology (CRM and DRM negative, complete or nearly compete TME specimen and no rectal perforations) was reported for 86% (647/752) of patients (Roodbeen 2020).

In a non-randomised comparative study of 2,393 patients, the proportion of patients who had a positive resection margin was 6% (18/312). This compared with 8% (17/205) for open TME, 5% (55/1,163) for laparoscopic TME and 3% (18/713) for robotic TME (p=0.002; Ose 2021).

Completeness of mesorectal excision

In the systematic review of 2,048 patients, complete mesorectal excision was reported in 77% of patients who had TaTME and 73% of patients who had laparoscopic TME (OR 1.43, 95% CI 0.84 to 2.46, p=0.19; I^2=58%, 14 studies; Hajibandeh, 2020).

In the non-randomised comparative study of 710 patients, the proportion of patients with a complete mesorectal specimen was 93% (318/344) with TaTME and 89% (242/366) with laparoscopic TME (p=0.1678; de Lacy 2020).

In a registry of 364 patients, 90% (n=306) had a complete TME specimen (Roodbeen 2019).

In a registry of 1,283 patients with malignant or benign disease, 82% (645/849) of patients with rectal cancer who had laparoscopic assisted TaTME had a complete TME specimen (Yao 2021).

In the randomised controlled trial of 100 patients, an incomplete mesorectum was reported for 12% (6/50) of patients who had TaTME and 12% (6/50) of patients who had laparoscopic TME (p=0.616; Denost 2018).

In a randomised controlled trial of 261 patients, all patients had a complete or nearly complete mesorectal resection (Zeng 2020).

In a randomised controlled trial of 64 patients, a complete or nearly complete mesorectum was reported for 97% (31/32) of patients who had TaTME and 91% (29/32) of patients who had laparoscopic TME (p=0.329; Ren 2021).

Number of harvested lymph nodes

In the systematic review of 2,048 patients, the mean number of harvested lymph nodes was 17.1 in the TaTME group and 16.9 in the laparoscopic group (MD 1.08, 95% CI 0.22 to 1.93, p=0.01; I^2=8%, 13 studies; Hajibandeh 2020).

In the registry of 364 patients, the median number of lymph nodes harvested was 17 (IQR 13 to 24; Roodbeen 2019).

In the registry of 1,283 patients the median number of lymph nodes harvested was 14 (range 0 to 51; Yao 2021).

In the randomised controlled trial of 261 patients, the median number of lymph nodes evaluated was 15 in the TaTME group and 16 in the laparoscopic TME group (p=0.069; Zeng 2020).

In the randomised controlled trial of 64 patients, the mean number of lymph nodes harvested was 20 in the TaTME group and 21 in the laparoscopic TME group (p=0.321; Ren 2021).

CRM

In the systematic review of 2,048 patients, the mean CRM was 10.7 mm in the TaTME group and 11.1 mm in the laparoscopic group (MD 0.36, 95% CI -0.91 to 1.63, p=0.58; I^2=76%, 9 studies; Hajibandeh 2020).

In the non-randomised comparative study of 710 patients, the median distance to the CRM was 10.0 mm with TaTME and 7.5 mm with laparoscopic TME (p=0.0131; de Lacy 2020).

In the randomised controlled trial of 64 patients, the distance to the CRM was 6.8 mm in the TaTME group and 5.2 mm in the laparoscopic group (p=0.039; Ren 2021).

Positive CRM

In the systematic review of 2,048 patients, a positive CRM was reported in 6% of patients who had TaTME compared with 8% in the laparoscopic group (OR 0.67, 95% CI 0.45 to 0.98, p=0.04; I^2=0%, 14 studies; Hajibandeh 2020).

In the registry of 364 patients, 10 patients had a positive CRM (Roodbeen 2019).

In the registry of 1,283 patients, a positive CRM was reported in 3% (22/849) of patients (Yao 2021).

In the non-randomised comparative study of 710 patients, the proportion of patients with a positive CRM was 10% (32/344) with TaTME and 16% (56/366) with laparoscopic TME (p=0.0038; de Lacy 2020).

In the randomised controlled trial of 100 patients, a positive CRM was reported in 4% (2/50) of patients who had TaTME and 18% (9/50) of patients who had laparoscopic TME (p=0.025; Denost 2018).

In the randomised controlled trial of 261 patients, a positive CRM was reported in 2% (2/128) of patients who had TaTME and 2% (2/133) of patients who had laparoscopic TME (p=0.674; Zeng 2020).

In the randomised controlled trial of 64 patients, a positive CRM was reported in 3% (1/32) of patients who had TaTME and 13% (4/32) of patients who had laparoscopic TME (p=0.355; Ren 2021).

DRM

In the systematic review of 2,048 patients, the mean DRM was 23.5 mm in the TaTME group and 21.7 mm in the laparoscopic group (MD 1.87, 95% CI -0.75 to 4.49, p=0.16; I^2=74%, 13 studies; Hajibandeh 2020).

In the non-randomised comparative study of 710 patients, the median distance to the DRM was 20.0 mm with TaTME and 19.5 mm with laparoscopic TME (p=0.248). The proportion of patients with a positive DRM was 1.8% (6/344) with TaTME and 2.0% (7/366) with laparoscopic TME (p=0.6135; de Lacy 2020).

In the registry of 364 patients, 4 patients had a positive DRM (Roodbeen 2019).

In the registry of 1,283 patients, the median DRM was 20 mm and a positive DRM was reported in 1% (6/849) of patients (Yao 2021).

In the randomised controlled trial of 261 patients, a positive DRM was reported in none of the patients who had TaTME and 2% (2/133) of patients who had laparoscopic TME (p=0.498; Zeng 2020).

Functional outcomes and quality of life

In a systematic review of 465 patients, the mean LARS score after the procedure was 30.6 in the TaTME group and 28.3 in the laparoscopic group (p=0.115, follow up not reported). Major or severe LARS occurred in 53% (129/242) of patients who had TaTME and 48% (107/223) of patients who had laparoscopic TME (OR 1.28, 95% CI 0.88 to 1.87, p=0.235). According to the EORTC QLQ-C29 scores, buttock pain, changes to taste, hair loss, faecal incontinence and sore skin were statistically significantly more common in the TaTME group compared with the laparoscopic group (p=0.011, 0.047, 0.010, 0.032, and 0.023 respectively). Abdominal pain and bloating symptoms were statistically significantly more common in the laparoscopic group (p=0.044 and 0.042 respectively). There were no statistically significant differences for any of the functional scales or in global health status scores across all studies (Choy 2021).

In the systematic review of 638 patients, the mean LARS score was statistically significantly higher in the TaTME group than in the laparoscopic TME group (weighted MD 2.88; 95% CI 0.15 to 5.60; p=0.04; I^2=0%; 4 studies). There were no statistically significant differences in mean Wexner score (2 studies) or IPSS (2 studies; Alimova 2021).

Safety summary

Conversion

Conversion to open surgery was reported in 1% of patients who had TaTME and 9% of patients who had laparoscopic TME (OR=0.17, 95% CI 0.10 to 0.29, p<0.00001, I^2=15%, 15 studies) in the systematic review of 2,048 patients (Hajibandeh 2020).

Conversion to an open procedure was reported in 1% (4/312) of patients who had TaTME, 11% (127/1,163) of patients who had laparoscopic TME and 6% (40/713) of patients who had robotic TME in the non-randomised comparative study of 2,393 patients (Ose 2021).

Abdominal conversion to an open procedure was reported in 7% of patients and perineal conversion in 3% of patients in the registry of 364 patients (Roodbeen 2019).

The conversion rate was 4% (26/608) in the cohort study of 608 patients (Caycedo-Marulanda 2021).

The conversion rate was less than 1% in the abdominal phase and 2% in the perineal phase in the registry of 1,283 patients (Yao, 2021).

Abdominal conversion to an open procedure was reported in 3% of patients and perineal conversion in 1% (11/767) of patients in the cohort study of 767 patients (Roodbeen 2020).

Anastomotic leak

Anastomotic leak was reported in 10% of patients who had TaTME and 11% of patients who had laparoscopic TME (p=0.61, 16 studies) in the systematic review of 2,048 patients (Hajibandeh 2020).

The pooled anastomotic leakage rate was 7% in a systematic review of 2,446 patients (An 2021).

Anastomotic leak was reported in 10% of patients who had TaTME and 12% of patients who had open, laparoscopic or robotic TME (p=0.698) in the non-randomised comparative study of 2,393 patients (Ose 2021).

Anastomotic leak was reported in 6% (7/128) of patients who had TaTME and 4% (5/133) of patients who had laparoscopic TME in the randomised controlled trial of 261 patients (Zeng 2020).

Anastomotic leak or abscess was reported in 2% (1/50) of patients who had TaTME and 10% (5/50) of patients who had laparoscopic TME (p=0.204) in the randomised controlled trial of 100 patients (Denost 2018).

Anastomotic leak within 30 days of the procedure was reported in 9% (26/289) of patients and anastomotic leak more than 30 days after the procedure was reported in 4% (10/289) of patients in the registry of 364 patients (Roodbeen 2019).

Anastomotic leak at discharge date was reported in 6% (44/796) of patients who had a primary anastomosis in the registry of 1,283 patients and 16 of these patients needed relaparotomy (Yao, 2021).

Anastomotic leak was reported in 8% (11/131) of patients in the cohort study of 157 patients (Wasmuth 2020).

Anastomotic leak within 30 days was reported in 8% (46/608) of patients in the cohort study of 608 patients (Caycedo-Marulanda 2021).

Infection

Surgical site infection was reported in 4% of patients who had TaTME and 5% of patients who had laparoscopic TME (p=0.26, 6 studies) in the systematic review of 2,048 patients (Hajibandeh 2020).

Pelvic abscess was reported in 1% of patients in the registry of 364 patients (Roodbeen 2019) and less than 1% (3/817) of patients in the registry of 1,283 patients (Yao 2021).

Peritonitis was reported in 1 patient who had TaTME and no patients who had laparoscopic TME in the randomised controlled trial of 261 patients (Zeng 2020).

Bleeding

Haemorrhage was reported in 6% (20/364) of patients in the registry of 364 patients (Roodbeen 2019).

Bleeding events needing conversion to open surgery were reported in 1% (2/157) of patients in the cohort study of 157 patients (Wasmuth 2020).

Bleeding was reported in 13% (70/548) of patients in the registry of 1,283 patients (Yao 2021).

Urethral injury

Urethral injury was reported in 1% (3/364) of patients in the registry of 364 patients (Roodbeen 2019) and 1% (2/157) of patients in the cohort study of 157 patients (Wasmuth 2020).

Ureter or urethral injury was reported in 1 patient each in the TaTME group and the laparoscopic TME group in the non-randomised comparative study of 792 patients who were propensity matched (Detering 2019).

Urethral injury was reported in 2 of 608 patients and 2 of 767 patients in 2 of the cohort studies (Caycedo-Marulanda 2021; Roodbeen 2020).

Urethral injury was reported in 1% (3/548) of patients in the registry of 1,283 patients (Yao, 2021).

Urological morbidity was reported in 6% (3/50) of patients who had TaTME and 10% (5/50) of patients who had laparoscopic TME in the randomised controlled trial of 100 patients (p=0.715; Denost 2018).

Bladder injury

Bladder injury was reported in 1 patient in the cohort study of 157 patients (Wasmuth 2020).

Vaginal injury

Vaginal injury was reported in 1 patient in the cohort study of 608 patients (Caycedo-Marulanda 2021).

Carbon dioxide embolism

Carbon dioxide embolism was reported in 1 patient in the registry of 364 patients (Roodbeen 2019).

Clinically relevant intraoperative carbon dioxide embolism was reported in less than 1% (2/767) of patients in the cohort study of 767 patients (Roodbeen 2020).

The incidence of clinically apparent carbon dioxide embolism was estimated to be about 0.4% (25/6,375) in a review of international registry data (Dickson 2019).

Rectal perforation

Intraoperative rectal perforation was reported in 5% (7/157) of patients in the cohort study of 157 patients (Wasmuth 2020).

Defects were made in the rectum in less than 1% (3/608) of patients in the cohort study of 608 patients, 1 of whom subsequently had a local recurrence (Caycedo-Marulanda 2021).

Rectal perforation was reported in 1% (2/344) of patients who had TaTME and 3% (8/366) of patients who had laparoscopic TME (p=0.0262) in the non-randomised comparative study of 710 patients (de Lacy 2020).

Rectal perforation was reported in 1% (8/766) of patients in the cohort study of 767 patients (Roodbeen 2020).

Mortality

Pooled 30-day mortality was 0.4% (95% CI 0.1 to 1.4%) in the systematic review of 2,446 patients (An 2021).

Mortality at 30 days was 1% (3/312) in patients who had TaTME, 0% (0/205) of patients who had open TME, 2% (21/1,163) of patients who had laparoscopic TME and 1% (6/713) of patients who had robotic TME (p=0.029) in the non-randomised comparative study of 2,393 patients (Ose 2021).

Mortality at 30 days was 4% (16/364) in the registry of 364 patients (Roodbeen 2019).

Overall, 30-day mortality was 3% (4/157) and mortality during the first 100 days after surgery was 3% (5/157) in the cohort study of 157 patients (Wasmuth 2020).

Mortality was reported in less than 1% (1/396) of patients in the TaTME group and 1% (3/396) of patients in the laparoscopic TME group (p=0.625) in the non-randomised comparative study of 792 propensity matched patients (Detering 2019).

Mortality at 30 days was 1% (4/608) of patients in the cohort study of 608 patients (Caycedo-Marulanda 2021).

Postoperative death was reported in 1 patient in the cohort study of 767 patients; the patient died on postoperative day 3 because of sepsis related to colonic ischaemia (Roodbeen 2020).

There were no deaths within 30 days in the randomised controlled trial of 261 patients (Zeng 2020).

Surgical reintervention

Surgical reintervention was reported in 8% of patients within 30 days and in 4% of patients more than 30 days after the procedure in the registry of 364 patients (Roodbeen 2019).

Reoperation was reported in 4% (2/50) of patients who had TaTME and 8% (4/50) of patients who had laparoscopic TME in the randomised controlled trial of 100 patients (Denost 2018; p=0.678).

Of the 32 patients who had a complication, 15% (2/13) who had TaTME and 37% (7/19) who had laparoscopic TME (p=0.353) needed another operation in the randomised controlled trial of 261 patients (Zeng 2020).

Readmission

Readmission within 30 days was reported in 6% of patients and readmission after more than 30 days was reported in 9% of patients in the registry of 364 patients (Roodbeen 2019).

Readmission was reported in 17% (68/396) of patients in the TaTME group and 19% (74/396) of patients in the laparoscopic TME group (p=0.640) in the non-randomised comparative study of 792 propensity matched patients (Detering 2019).

Readmission was reported in 16% (100/608) of patients in the cohort study of 608 patients (Caycedo-Marulanda 2021).

Readmission within 30 days was reported in 8% (61/767) of patients in the cohort study of 767 patients (Roodbeen 2020).

Other

A possible case of port-site metastasis after TaTME was described in a case report (Perdawood 2018).

Colonic conduit prolapse after TaTME for low rectal cancer was described in 4 case reports (Balaphas 2018).

Anecdotal and theoretical adverse events

In addition to safety outcomes reported in the literature, professional experts are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never happened). For this procedure, professional experts did not list any additional anecdotal or theoretical events.

The evidence assessed

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to TaTME for rectal cancer. The following databases were searched, covering the period from their start to 13 August 2021: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see the literature search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The inclusion criteria were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with rectal cancer.
Intervention/test	Transanal total mesorectal excision
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the IP overview

This IP overview is based on about 6,000 patients who had TaTME from 4 systematic reviews, 2 registry reports, 3 non-randomised comparative studies (1 of which was also included in a systematic review), 4 cohort studies, 3 randomised controlled trials, 1 case series and 2 case reports (Hajibandeh 2020; Choy 2021; Roodbeen 2019; Wasmuth 2020; Detering 2019;

de Lacy 2020; Caycedo-Marulanda 2021; Yao 2021; Roodbeen 2020; Denost 2018; Zeng 2020; Ren 2021; Dickson 2019; Perdawood 2018; Balaphas 2018; Alimova 2021; An 2021; Ose 2021; Van Oostendorp 2021).

Other studies that were considered to be relevant to the procedure but were not included in the main summary of the key evidence are listed in the appendix.

Summary of key evidence on transanal total mesorectal excision for rectal cancer

Study 1 Hajibandeh S (2020)

Study details

Study type	Systematic review
Country	Included studies were from the Netherlands, Spain, France, Denmark, Taiwan, Russia, US, Italy, Poland
Recruitment period	Search date: November 2019
Study population and number	n=2,048 patients (1,000 TaTME, 1,048 laparoscopic TME); 18 studies Patients with low or middle rectal cancer
Age and sex	Mean or median age ranged from 55 to 70 years (TaTME) and 58 to 70 years (laparoscopic TME); the proportion of males ranged from 33% to 83% (TaTME) and from 47% to 78% (laparoscopic TME).
Patient selection criteria	All randomised and non-randomised studies evaluating the outcomes of TaTME and laparoscopic TME in patients with low or middle rectal cancer were included. Low rectal cancer was defined as cancer within 6 cm of anal verge, and middle rectal cancer was defined as cancer within 6 and 11 cm from anal verge. Patients aged over 18 years of any gender who had transanal or laparoscopic TME for rectal cancer were considered.
Technique	TaTME compared with laparoscopic TME.
Follow up	Not reported
Conflict of interest/source of funding	Not reported

Analysis

Study design issues: Systematic review and meta-analysis, done in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement standards. One randomised controlled trial and 17 retrospective observational studies were included. Methodological quality and risk of bias were assessed using the Newcastle-Ottawa scale for observational studies and Cochrane's tool for randomised studies. The risk of bias was judged as low in 8 observational studies and moderate in the remaining 9. The unit of analysis in this study was individual participants. The final analysis was based on the intention-to-treat concept. A subanalysis was done on patients with low rectal tumours.

Study population issues: There were no statistically significant differences between the groups for age, gender and mean body mass index. The number of patients with rectal cancer stage 2 was statistically significantly higher in the laparoscopic group (p=0.01). In the 10 studies that reported it, the mean distance from the distal tumour to anal verge was 6.05 cm in the transanal group and 7.12 cm in the laparoscopic group (p=0.18). The proportion of patients who had neoadjuvant chemotherapy was similar between the 2 groups.

Key efficacy findings

Number of patients analysed: 2,048 (1,000 TaTME, 1,048 laparoscopic TME)

R0 resection (17 studies, n=1,976)

- TaTME=95.9%
- Laparoscopic TME=93.2%, OR=1.67, 95% CI 1.12 to 2.50, p=0.01 (I^2=0%, p=0.82)

For patients with low rectal tumours (n=435), OR=1.78, 95% CI 0.85 to 3.69, p=0.12 (I^2=0%, p=0.91)

Completeness of mesorectal excision (14 studies, n=988)

- TaTME=77.1% (n=380)
- Laparoscopic TME=73.1% (n=362), OR=1.43, 95% CI 0.84 to 2.46, p=0.19 (I^2=58%, p=0.003)

For patients with low rectal tumours (n=435), OR=1.34, 95% CI 0.56 to 3.18, p=0.51 (I^2=69%, p=0.003)

Number of harvested lymph nodes (13 studies, n=1,026)

- TaTME=17.1±4.2
- Laparoscopic TME=16.9±4.6, MD=1.08, 95% CI 0.22 to 1.93, p=0.01 (I^2=8%, p=0.37)

For patients with low rectal tumours (n=331), MD=2.06, 95% CI 0.79 to 3.33, p=0.002 (I^2=32%, p=0.21)

DRM (13 studies, n=1,024)

- TaTME=23.5±9.1 mm
- Laparoscopic TME=21.7±8.8 mm, MD=1.87, 95% CI -0.75 to 4.49, p=0.16 (I^2=74%, p<0.0001)

For patients with low rectal tumours (n=329), MD=-0.47, 95% CI -1.88 to 0.94, p=0.52 (I^2=0%, p=0.57)

CRM (9 studies, n=773)

- TaTME=10.7±1.3 mm
- Laparoscopic TME=11.1±2.5 mm, MD=0.36, 95% CI -0.91 to 1.63, p=0.58 (I^2=76%, p<0.0001)

For patients with low rectal tumours (n=216), MD=0.58, 95% CI -2.87 to 4.03, p=0.74 (I^2=74%, p=0.003)

Positive CRM (14 studies, n=1,809)

- TaTME=6.1%
- Laparoscopic TME=8.4%, OR=0.67, 95% CI 0.45 to 0.98, p=0.04 (I^2=0%, p=0.76)

For patients with low rectal tumours (n=301), OR=0.78, 95% CI 0.41 to 1.49, p=0.45 (I^2=0%, p=0.90)

Key safety findings

Conversion to open (15 studies, n=1,911)

- TaTME=1.4%
- Laparoscopic TME=8.8%, OR=0.17, 95% CI 0.10 to 0.29, p<0.00001 (I^2=15%, p=0.30)

For patients with low rectal tumours (n=507), OR=0.28, 95% CI 0.12 to 0.65, p=0.003 (I^2=28%, p=0.22)

Intraoperative complications (11 studies, n=870)

- TaTME=7.5% (n=31)
- Laparoscopic TME=6.3% (n=29), OR=1.18, 95% CI 0.69 to 2.01, p=0.54 (I^2=0%, p=0.66)

In the TaTME group, intraoperative complications included bleeding, vaginal injury, bowel perforation, rectal perforation, bladder injury, urethral injury, intraoperative anastomotic leak.

In the laparoscopic group, intraoperative complications included bleeding, bowel perforation, rectal perforation, ureter injury, small bowel injury, intraoperative anastomotic leak.

For low rectal tumours only (n=363), OR=1.52, 95% CI 0.62 to 3.76, p=0.36 (I^2=28%, p=0.24).

Postoperative complications (17 studies, n=1,998)

- TaTME=34.7% (n=338)
- Laparoscopic TME=36.3% (n=371), OR=0.89, 95% CI 0.74 to 1.08, p=0.24 (I^2=43%, p=0.03)

For low rectal tumours only (n=507), OR=0.92, 95% CI 0.63 to 1.33, p=0.65 (I^2=0%, p=0.80).

Anastomotic leak (16 studies, n=1,744)

- TaTME=9.9%
- Laparoscopic TME=10.5%, OR=0.88, 95% CI 0.64 to 1.20, p=0.42 (I^2=0%, p=0.61)

For low rectal tumours only (n=480), OR=0.47, 95% CI 0.24 to 0.92, p=0.03 (I^2=0%, p=0.82).

Surgical site infections (6 studies, n=577)

- TaTME=3.8% (n=10)
- Laparoscopic TME=5.4% (n=17), OR=0.64, 95% CI 0.30 to 1.38, p=0.26 (I^2=0%, p=0.73)

For low rectal tumours only (n=177), OR=2.07, 95% CI 0.37 to 11.57, p=0.41 (I^2=0%, p=0.82).

Study 2 Choy K (2021)

Study details

Study type	Systematic review
Country	Included studies were from Hong Kong, Denmark, Poland, China, Spain, Netherlands and France
Recruitment period	Search date: August 2020
Study population and number	n=465 (242 TaTME, 223 laparoscopic TME); 7 studies
Age and sex	• TaTME: mean age range 57.5 to 68 years; 68% male • Laparoscopic TME: mean age range 59.9 to 68 years; 62% male
Patient selection criteria	The following medical subject heading terms and text words were used for the search in all possible combinations: "(rectal neoplasm OR cancer)" AND "(transanal TME OR laparoscopic TME)" AND "function" OR "functional outcomes". All articles comparing functional outcomes after TaTME and laparoscopic TME in adult populations were included. All non-English studies, letters, perspectives, conference abstracts, or studies focusing on paediatric patients were excluded.
Technique	TaTME or laparoscopic TME.
Follow up	Not reported
Conflict of interest/source of funding	None

Analysis

Study design issues: Systematic review and meta-analysis comparing functional outcomes between TaTME and laparoscopic TME. There was 1 randomised controlled trial and 6 non-randomised studies (3 prospective and 3 retrospective). All studies were deemed to be good quality studies. Outcome measures included the LARS score, the Jorge-Wexner scale to measure severity of faecal incontinence, the IPSS, and the EORTC QLQ (QLQ C-29/30).

Study population issues: All studies included patients who had neoadjuvant chemoradiotherapy, with a slightly lower proportion of 44% (107 patients) in the TaTME group compared with 50% (112 patients) in the laparoscopic group. In the 4 studies that reported tumour staging, there were 46 (37%) patients in the TaTME group and 58 (54%) patients in the laparoscopic TME group, who had at least stage 3a or Dukes C colorectal cancer.

Key efficacy findings

Number of patients analysed: 465 (242 TaTME, 223 laparoscopic TME)

Functional outcome assessment

LARS score (7 studies); scale 0 to 42, higher scores indicate more severe symptoms

- Mean LARS score in TaTME group=30.6
- Mean LARS score in laparoscopic TME group=28.3
- 53.3% (129/242) of patients who had TaTME had major or severe LARS compared with 48.0% (107/223) of patients who had laparoscopic TME (OR 1.28, 95% CI 0.88 to 1.87, p=0.235)

There was no statistically significant difference between the groups, with the standard MD (SMD) favouring the TaTME group (SMD 0.42, 95% CI −0.10 to 0.93, p=0.115).

Jorge-Wexner scale (3 studies); scale 0 to 20, higher scores indicate more severe symptoms

- Score range in TaTME group=7 to 9
- Score range in laparoscopic group=7 to 10

There was no statistically significant difference between the groups with the SMD favouring the TaTME group (SMD 0.09, 95% CI −0.26 to 0.43, p=0.623).

IPSS (3 studies); scale 0 to 35, higher scores indicate more severe symptoms

- Score range in TaTME group=5.5 to 8
- Score range in laparoscopic group=3.5 to 10.1
- 28.1% (32 patients) in the TaTME group and 25.8% (25 patients) in the laparoscopic group had moderate or severe IPSS symptoms (OR 1.11, 95% CI 0.60 to 2.06, p=0.851)

There was no statistically significant difference between the 2 groups with the SMD favouring the TaTME group (SMD 0.07, 95% CI − 0.56 to 0.69, p=0.835).

EORTC QLQ-C29 (3 studies)

Buttock pain, changes to taste, hair loss, faecal incontinence, and sore skin were statistically significantly more common in the TaTME group (p=0.011, 0.047, 0.010, 0.032, and 0.023 respectively).

Abdominal pain and bloating symptoms were statistically significantly more common in the laparoscopic group (p=0.044 and 0.042 respectively). There were no statistically significant differences for any of the functional scales.

EORTC QLQ-C30 (3 studies)

Diarrhoea, fatigue, and financial difficulties were statistically significantly more common in the laparoscopic group (p=0.009, 0.021, and 0.032 respectively).

Role functioning was statistically significantly affected in favour of the laparoscopic group (p=0.042).

There were no statistically significant differences in global health status scores across all studies.

Key safety findings

Complication rate (3 studies)

- TaTME=10.2% (n=9)
- Laparoscopic=16.7% (n=14), OR 0.58, 95% CI 0.23 to 1.42, p=0.332

Study 3 Roodbeen S (2019)

Study details

Study type	Registry (TaTME registry)
Country	UK (42 surgical units)
Recruitment period	2013 to 2018
Study population and number	n=364 patients with rectal cancer (149 patients with benign pathology were also included) Patients who had TaTME for benign or malignant indications
Age and sex	For patients with cancer, median age was 67 years and 77% (280/364) were male
Patient selection criteria	UK patients who had TaTME for benign or malignant indications.
Technique	The most common procedure in the cancer group was anterior resection (83%). Simultaneous 2-team operating was done in 41% (150/364) of patients with cancer. Laparoscopy was the most common abdominal approach (98%) and a Gelpoint platform (Applied Medical, US) was used for 94% of procedures. Other platforms used were TEO (Karl Storz Endoskope), TEM (Richard Wolf) and Glove port. A defunctioning stoma was created in 95% of patients who had a restorative procedure in the cancer group. Neoadjuvant therapy was given to 35% (129/364) of patients, mostly as long course chemoradiotherapy.
Follow up	Mean 5 months
Conflict of interest/source of funding	One author has received speaking fees from Applied Medical. The Pelican Cancer Foundation has funded the registry.

Analysis

Study design issues: The TaTME is an international secure online voluntary database. In addition to the database, a survey was also sent to surgeons in the UK who have had training on TaTME. The primary endpoint was a composite for 'optimal pathology' (clear resection margins [R0] and complete or nearly complete TME specimen and no rectal perforations). Secondary outcomes included 30-day clinical course and surgeons experience with implementing TaTME according to the survey. Reported percentages exclude missing values.

Study population issues: The American Society of Anesthesiologists score was 3 or higher in 21% (76/364) of patients in the cancer group. Median tumour height from anorectal junction on staging MRI was 4 cm. Tumours were staged as 3 or higher in 68% (241/364) of patients and nodal status was 1 or more in 46% (164/364) of patients. Preoperative involvement of the CRM was seen on MRI in 28% (101/364) of patients.

Other issues: Of the 42 surgical units, 22 (52%) had 0 to 5 cases and 6 (14%) had more than 20 cases. In total, 79% (68/86) of surgeons responded to the training survey. 76% (51/67) of surgeons stated they had adopted the technique in their unit, all of whom reported encountering difficulties during a procedure.

This study is included in the systematic review by An et al. (2021)

Key efficacy findings

Number of patients analysed: 364

- Composite optimal pathology=92.8% (n=295, denominator not stated)
- Complete TME specimen=90.3% (n=306, denominator not stated)
- Positive resection margin (R1)=4.1% (n=13, denominator not stated)
  - Positive CRM, n=10
  - Positive DRM, n=4
- Median number of lymph nodes harvested=17 (IQR 13 to 24)

Histopathological outcomes – cancer stage

Parameters	n (%)
pT stage – no residual tumour	32 (9.3)
T1	25 (7.2)
T2	6 (1.7)
T3	277 (80.3)
T4	5 (1.4)
pN stage – N0	227 (65.8)
N1	81 (23.5)
N2	37 (10.7)

Key safety findings

Perioperative complications

- Abdominal conversion to open procedure=6.7% (n=22)
- Perineal conversion (change in approach from transanal to a more extensive abdominal approach than initially planned)=3% (n=10)
- Blood loss more than 500 ml=4.6% (n=16)
- Haemorrhage=5.5% (20/364)
- Pneumopelvis=6.0% (22/364)
- Poor smoke evacuation=6.0% (22/364)
- Poor platform seal=5.2% (19/364)
- Incorrect plane entering=7.7% (28/364)
- Urethral injury=1.0% (3/364)
- CO_2 embolism=0.3% (1/364)

Postoperative outcomes

- 30-day morbidity=38.6% (n=130)
- Clavien-Dindo 3 or higher within 30 days=13.4% (n=45)
- 30-day mortality=4.4% (16/364; 2 patients had multiorgan failure, 1 had an anastomotic leakage and 1 had a small bowel injury intraoperatively that was not seen during the procedure.)

- Anastomotic failure=13.9% (40/289)
- Anastomotic leak within 30 days=9.0% (26/289)
- Anastomotic leak more than 30 days after procedure=3.5% (10/289)
- Pelvic abscess=1.4% (n=4)
- Surgical reintervention within 30 days=7.7% (n=28)
- Surgical reintervention more than 30 days after procedure=3.6% (n=12)
- Readmission within 30 days=5.8% (n=21)
- Readmission after more than 30 days=8.8% (n=32)

Study 4 Wasmuth H (2020)

Study details

Study type	Cohort study
Country	Norway (7 centres)
Recruitment period	2014 to 2018
Study population and number	n=157 Patients with rectal cancer
Age and sex	Mean 65 years; 69% (109/157) male
Patient selection criteria	All patients with rectal cancer who had TaTME were included.
Technique	The transanal approach was done using a platform for transanal microsurgery. Eight operations were completion procedures after transanal minimally invasive surgery/transanal endoscopic microsurgery (n=7), or endoscopic polypectomy (n=1). The remaining 149 procedures were primary resections. Two teams operated simultaneously in all but 9 patients. 33 (21%) patients had preoperative chemoradiotherapy.
Follow up	Median 19.5 months (range 0 to 51)
Conflict of interest/source of funding	1 author received travel grants from Medtronic.

Analysis

Study design issues: All patients with rectal cancer in Norway were aggregated in a national database if they were reported as having a TaTME procedure by the performing hospital. The primary endpoint was the local recurrence rate. Secondary outcomes were rates of involved CRM, early postoperative death, anastomotic leak and stoma. Patients who died within 100 days after surgery were excluded from the statistical analysis of local recurrence estimates.

Oncological results were compared with data from the NCCR relating to a corresponding cohort of patients with stage 1 to 3 rectal cancer treated by open or laparoscopic rectal resection procedures from 2015 to 2018, matched according to distance from the tumour to anal verge and T and N categories. Early anastomotic leak rates for the TaTME cohort were compared with results from the NoRGast for patients who had low anterior resection for rectal cancer between 2015 and 2018. Only grade C leaks that needed reoperation were compared.

Study population issues: The tumour distance from the anal verge on rigid proctoscopy ranged from 2 to 13 cm (median 8). Mean tumour size was 3·8 cm (range 0·8–10·0) on MRI. Of the 153 tumours with data on the position, 9 (6%) were low, 126 (82%) were in the middle and 18 (12%) were high.

Other issues: Of the 7 hospitals, 4 were defined as high-volume and accounted for 152 (range 32–57) procedures. The other 3 hospitals abandoned TaTME after between 1 and 3 procedures.

Key efficacy findings

Number of patients analysed: 157

Postoperative histology: pathological tumour and node categories, n (%)

Histology category	TaTME cohort	NCCR cohort	p
Tumour category	n=157	n=1175	0.001
ypt0*	8 (5.1)	71 (6.0)	
pT1	27 (17.2)	98 (8.3)	
pT2	57 (36.3)	389 (33.1)	
pT3	57 (36.3)	573 (48.7)	
pT4	8 (5.1)	44 (3.7)	
Node category	n=157	n=1106	0.371
pN0	108 (68.8)	736 (66.5)	
pN1	29 (18.5)	259 (23.4)	
pN2	20 (12.7)	111 (10.0)	

* Pathological complete response after chemoradiotherapy

- Local recurrence in TaTME cohort=7.9% (12/152); 3 patients had concurrent metastases

Of the 12 patients with local recurrences, 4 had R1 resections and 8 had R0 resections. The recurrences were described as multifocal in 6 patients and extensive in 2; 1 was in the staple line and 1 presacral. The recurrence in the other 2 patients was described as probably being derived from the pelvic lymph nodes. Only 1 patient diagnosed with local recurrence had preoperative chemoradiotherapy.

All recurrences in the TaTME cohort occurred within 2 years after surgery, with a median of 9·5 months (range 2 to 23) months.

The univariable HR for local recurrence after TaTME compared with the national cohort was 5·70 (95% CI 2·70 to 12·06, p<0·001). Adjusting for sex, age and chemoradiotherapy did not change the HR. Adjusting for tumour distance from the anal verge, pT and pN category increased the HR to 6·71 (95% CI 2·94 to 15·32; p<0·001).

Stomas

A Hartmann's procedure was planned in 16 patients because of low tumour position, incontinence or frailty. An intraoperative decision was made to convert to a stoma procedure in 10 patients because of complications such as bleeding or technical problems. Postoperative complications or anastomotic failures led to permanent stoma formation in a further 13 patients.

Permanent stoma=24.8% (39/157)

The final rate of Hartmann's procedure was 11·5% (18/157) compared with 9·0% (196/2,186) in the NCCR cohort (p=0·07).

Key safety findings

- Mortality during follow up=10.2% (16/157)

Complications

- Intraoperative rectal perforation=4.5% (7/157)
- Urethral injury=1.3% (2/157)
- Bladder injury=0.6% (1/157)
- Bleeding events needing conversion to open surgery=1.3% (2/157)
- Anastomotic leak=8.4% (11/131; compared with 4.5% [56/1,230] in NoRGast, p=0.047)
- Overall, 30-day mortality=2.5% (4/157; compared with 0.4% [8/2,026] after all rectal cancer resections reported to NoRGast in the same interval, p=0.008)
- 30-day mortality in patients with an anastomosis=2.3% (3/131; compared with 0.3% [4/1,230] in NoRGast, p=0.019)
- Mortality during the first 100 days after primary surgery=3.2% (5/157; compared with 1.3% [15/1,188] in the corresponding NCCR cohort, p=0.051).

Study 5 Detering R (2019)

Study details

Study type	Non-randomised comparative study (propensity score matched)
Country	The Netherlands
Recruitment period	2015 to 2017
Study population and number	n=3,777 (416 TaTME, 3,361 laparoscopic TME); 792 matched patients (396 in each group) Patients with primary rectal cancer
Age and sex	Before matching, 82.5% of patients in the TaTME group were younger than 75 compared with 75.8% in the laparoscopic group (p=0.003); 72.4% of patients in the TaTME group were male compared with 63.8% in the laparoscopic group (p=0.001).
Patient selection criteria	All patients who TaTME or laparoscopic TME for primary rectal cancer and were registered in the Dutch ColoRectal Audit were included. A patient was eligible for analysis when information on the location of the tumour, date of surgery, and status of the patient was known (30-day or in-hospital mortality). Exclusion criteria were tumours more than 10 cm from the anorectal junction, previous local excision, and an emergency setting. Abdominoperineal resections were excluded.
Technique	TaTME or laparoscopic TME. If a combined endoscopic transanal and laparoscopic approach was registered, this was considered TaTME. Laparoscopic TME included procedures done by only a transabdominal laparoscopic approach.
Follow up	30 days
Conflict of interest/source of funding	None

Analysis

Study design issues: Multicentre propensity matched cohort study. Data were derived from the Dutch ColoRectal Audit, a mandatory nationwide registry in which information on patient, tumour, intraoperative details, and short-term outcomes (within 30 days) of all patients with primary colorectal cancer having resection is collected. Propensity matching used 7 factors (sex, body mass index, tumour height, cTNM-stage, preoperative threatened margin on MRI, neoadjuvant therapy, and operation year). Preoperative threatened margin on MRI was defined as the presence of tumour or malignant lymph nodes 1 mm or less from the mesorectal fascia. The primary outcome was CRM involvement, defined as the presence of tumour or malignant lymph node 1 mm or less from the margin. Secondary endpoints included proportion of primary anastomosis, diverting stoma, laparoscopic conversion, intraoperative complications, and short-term postoperative outcomes (overall complications, anastomotic leakages, length of postoperative hospital stay, complicated course, readmission, and mortality). Missing data did not exceed 15% for the variables presented.

Study population issues: Relatively more males and younger patients were represented in the TaTME group. Patients in the TaTME group had less preoperative therapy than those who had laparoscopic TME (36% compared with 42%, p<0.001). Preoperative threatened margin on MRI was higher in the TaTME group (32% compared with 24%, p=0.004), and the proportion of low tumours was higher in the TaTME group (26%

compared with 9.5%, p<0.001). After matching, there were no statistically significant differences in baseline characteristics between the groups.

Other issues: Transanal TME was done in 38 hospitals, of which 18 (47%) hospitals had 0 to 5 TaTME cases, 8 (21%) hospitals had 6 to 10 cases, 6 (16%) hospitals had 11 to 20 cases, and 6 (16%) hospitals had more than 20 cases. Laparoscopic TME was done in 90 hospitals, 64 (71%) of which had more than 20 cases.

This study is also included in the systematic reviews by Hajibandeh et al. (2020) and An et al. (2021).

Key efficacy findings

Number of patients analysed: 3,777 (416 TaTME, 3,361 laparoscopic TME)

Operative and pathologic outcome, n (%)

Outcome	**Before matching**			**After matching**		
	TaTME, n=416	Laparoscopic TME, n=3,361	p	TaTME, n=396	Laparoscopic TME, n=396	p
Anastomosis and stoma	122 (29.7)	1,130 (34.2)	0.035	116 (29.7)	112 (28.9)	0.351
Anastomosis, without stoma	210 (51.1)	1,405 (42.5)		199 (50.4)	175 (45.2)	
Hartmann's	79 (19.2)	772 (23.3)		76 (19.4)	100 (25.8)	
Missing, n	5	54		5	9	
pT stage, (y)pT0	34 (8.2)	226 (6.7)	0.421	33 (8.3)	39 (9.8)	0.295
(y)pT1	45 (10.8)	435 (13.0)		40 (10.1)	46 (11.6)	
(y)pT2	152 (36.5)	1,121 (33.5)		144 (36.4)	148 (37.4)	
(y)pT3	180 (43.3)	1,490 (44.5)		174 (43.9)	156 (39.4)	
(y)pT4	4 (1.0)	67 (2.0)		4 (1.0)	4 (1.0)	
(y)pTX	1 (0.2)	10 (0.3)		1 (0.3)	3 (0.8)	
missing, n	0	10		0	0	
pN stage, (y)pN0	271 (65.1)	2,236 (66.7)	0.073	258 (65.3)	291 (73.7)	0.012
(y)pN1	89 (21.4)	805 (24.0)		84 (21.3)	78 (19.7)	
(y)pN2	56 (13.5)	308 (9.2)		53 (13.4)	26 (6.6)	
(y)pNX	0 (0)	2 (0.1)		0 (0)	0 (0)	
Missing, n	0	9		1	1	
CRM positive	18 (4.4)	98 (3.0)	0.132	17 (4.3)	16 (4.0)	1.00
CRM negative	390 (95.6)	3,142 (97.0)		379 (95.7)	380 (96.0)	
More than 10 lymph nodes retrieved	345 (82.9)	2,763 (82.2)	0.587	334 (84.3)	320 (80.8)	0.227

Percentages are calculated out of the total number of actual results available, excluding the missing values. CRM positive rates were calculated after exclusion of (y)pT0N0 stage.

For TaTME, preoperative threatened margin on MRI and conversion were identified as independent risk factors for CRM involvement (OR 5.48, 95% CI 1.33 to 22.54 and OR 30.12, 95% CI 3.70 to 245.20, respectively).

For laparoscopic TME, 4 independent factors predisposing for CRM involvement were found: preoperative threatened margin on MRI (OR 1.99, 95% CI 1.18 to 3), multivisceral resection (OR 4.11, 95% CI 1.77 to 9.55), (y)pT-stage (OR 4.47, 95% CI 1.95 to 10.24), and (y)pN-stage (OR 4.84, 95% CI 3.03 to 7.75).

Key safety findings

Conversion rates, intraoperative complications and postoperative outcomes (within 30 days), n (%)

Outcome	**Before matching**			**After matching**		
	TaTME, n=416	Laparoscopic TME, n=3,361	p	TaTME, n=396	Laparoscopic TME, n=396	p
Conversion	6 (1.4)	292 (8.7)	<0.001	6 (1.5)	34 (8.6)	<0.001
Intraoperative complication	401 (96.4)	3,254 (96.8)	0.507	381 (96.2)	387 (97.7)	0.307
Ureter or urethra injury	1 (0.2)	6 (0.2)		1 (0.3)	1 (0.3)	
Other organ injury	14 (3.4)	82 (2.4)		14 (3.5)	8 (2.0)	
Bleeding needing transfusion	0 (0)	14 (0.4)		0 (0)	0 (0)	
Missing	0	5		0	0	
Multivisceral resection	9 (2.2)	61 (1.8)	0.620	9 (2.3)	5 (1.3)	0.388
Missing	0	1		0	0	
Postoperative outcome						
Overall complication	176 (42.3)	1,213 (36.1)	0.042	168 (42.4)	146 (36.9)	0.135
Anastomotic leakage	53/332 (16.0)	289/2,535 (11.4)	0.013	52/315 (16.5)	35/287 (12.2)	0.116
Complicated course	109 (26.2)	703 (20.9)	0.013	107 (27.0)	86 (21.7)	0.099
Readmission	71 (17.1)	517 (15.4)	0.371	68 (17.2)	74 (18.7)	0.640
Mortality	1 (0.2)	41 (1.2)	0.072	1 (0.3)	3 (0.8)	0.625

Anastomotic leakage was calculated after excluding patients with a permanent stoma without anastomosis.

The cause of the 4 deaths in the matched group was unknown.

Study 6 de Lacy F (2020)

Study details

Study type	Non-randomised comparative study
Country	Spain and the Netherlands
Recruitment period	2000 to 2018
Study population and number	n=710 (344 TaTME, 366 laparoscopic TME) Patients with primary locally advanced rectal adenocarcinoma
Age and sex	Mean 66 years; 66% (469/710) male
Patient selection criteria	Adult patients with a solitary locally advanced rectal adenocarcinoma (cT3/cT4, or cN1/cN2 with any cT) detected by MRI with or without transrectal ultrasonography, within 12 cm of the anal verge treated with TaTME or laparoscopic TME were included. Exclusion criteria: patients with cTisN0 or cT1-2 N0; pelvic malignancy within 5 years; severe, incapacitating disease (American Society of Anaesthesiologists classification 4 to 5; procedures done in an emergency setting; tumours previously treated by local excision; unknown cT or cM; metastatic tumours; synchronous tumours; active Crohn's or ulcerative colitis; familial risk-colorectal cancer syndromes; and patients with 30-day mortality when it was judged to have been a direct result of a major active postoperative complication, which was not of primary interest.
Technique	TaTME or laparoscopic TME. Tumours were considered high if the distal border of the tumour was more than 10 cm from the anal verge, mid if it was between 5 and 10 cm, and low in case of a distal border less than 5 cm. Patients were eligible for neoadjuvant therapy in cases of cT3b-d/cT4 or cN positive tumours below the peritoneal reflection, or if the CRM was threatened or involved, although other factors such as extramural venous invasion were also considered.
Follow up	Median follow up was 28.4 months (range 0.1 to 83.6) in the TaTME cohort and 61.1 months (range 1.1 to 205.7) in the laparoscopic TME cohort.
Conflict of interest/source of funding	9 of the 15 authors have no conflicts of interest or financial ties to disclose. One author reports an educational grant from Stryker, personal fees from Applied Medical outside the submitted work. One author reports personal fees from Medtronic, personal fees from Olympus, and personal fees from AFS medical, outside the submitted work. One author reports personal fees from Amadix, Goodgut and Universal Diagnostics, and grants from SAF2014 and AECC, outside the submitted work. One author reports grant from VIFOR, grants from Medtronic, and grants from Braun, outside the submitted work. One author reports personal fees from Johnson & Johnson, personal fees from Olympus, and personal fees from B Braun, and research grant from Life Cell, outside the submitted work. One author reports personal fees from Medtronic, personal fees from Olympus, personal fees from Applied Medical, and personal fees from Conmed, outside the submitted work.

Analysis

Follow up issues: Until follow up was completed after 5 years, patients visited every 3 to 6 months during the first 2 years and every 6 to 12 months during the remaining 3 years. An additional 153 patients were eligible for inclusion into the study but were excluded because of missing data.

Study design issues: Multicentre non-randomised comparative study. All patients with histologically proven rectal adenocarcinoma treated by TaTME were prospectively registered in a local standardised database or in the International TaTME Registry. A multicentre database was created, which included the TaTME cohort, and a cohort of patients having treatment by laparoscopic TME, through a retrospective analysis of clinical records. The primary endpoint was 3-year locoregional recurrence. Secondary endpoints included systemic recurrence, disease-free survival, and overall survival. An inverse probability of treatment weights approach was used. Sphincter saving surgery was not included in the inverse probability of treatment weighting because there was a large difference between the groups; it was used as an adjustment cofactor in Cox models.

Study population issues: The mean body mass index was 25.5 kg/m^2 in the TaTME group and 26.4 kg/m2 in the laparoscopic group. The mean distance from the anal verge was 7.2 and 6.5 cm respectively. The proportion of patients who had sphincter saving surgery was 97% in the TaTME group and 74% in the laparoscopic group. There were similar rates of neoadjuvant therapy in the 2 groups (71% compared with 77%, p=0.086). Abdominoperineal resection rates were statistically significantly lower in the TaTME group (3% compared with 26%, p<0.001).

Key efficacy findings

Number of patients analysed: 710

Pathological outcomes after inverse probability of treatment weighting

Outcome	TaTME, n=344	Laparoscopic TME, n=366	p value
Pathological stage (American Joint Committee on Cancer), n (%)			
0	38 (11.0)	32 (8.7)	0.8616
1	90 (26.1)	92 (25.1)	-
2	123 (35.7)	119 (32.5)	-
3	93 (27.0)	123 (33.6)	-
4	0 (0.0)	0 (0.0)	-
Mesorectal specimen, n (%)			
Complete	318 (93.2)	242 (89.3)	0.1678
Near complete	20 (5.8)	13 (4.8)	-
Incomplete	3 (0.8)	16 (5.9)	-
Distance to CRM, mm (median, 95% CI)	10.0 (10.0 to 12.0)	7.5 (6.0 to 10.0)	0.0131
CRM involvement, n (%)	32 (9.5)	56 (16.2)	0.0038
Distance to DRM, mm (median, 95% CI)	20.0 (20.0 to 25.0)	19.5 (15.0 to 20.0)	0.248
DRM involvement, n (%)	6 (1.8)	7 (2.0)	0.6135
Rectal perforation	2 (0.8)	8 (3.2)	0.0262
Composite poor pathological outcome	35 (10.6)	69 (24.7)	<0.001

Perineural invasion	44 (13.0)	47 (18.3)	0.0109
Lymphovascular invasion	68 (21.4)	44 (17.0)	0.0182
Budding			
No	155 (82.8)	38 (52.7)	0.0002
Low	23 (12.3)	32 (44.4)	-
Moderate	2 (1.0)	0 (0.0)	-
High	7 (3.7)	2 (2.7)	-
Differential grade			
Good	20 (6.3)	15 (4.8)	0.5589
Moderate	254 (80.3)	240 (77.4)	-
Poor	17 (5.3)	22 (7.1)	-
Number of lymph nodes harvested (median, 95% CI)	15.0 (15.0 to 16.0)	14.0 (14.0 to 15.0)	0.0133

Locoregional recurrence at 3-year follow up

- TaTME=3.6% (95% CI 1.1 to 6.1)
- Laparoscopic TME=9.6% (95% CI 6.5 to 12.7), HR=0.4 (95% CI 0.23 to 0.69, p=0.001)

For patients who had TaTME with sphincter preservation, HR=0.42 (95% CI 0.24 to 0.73, p=0.002).
For patients with low rectal cancer, HR=0.9 (95% CI 0.28 to 2.93, p=0.866).
For patients with cancer of the mid rectum, HR=0.39 (95% CI 0.2 to 0.76, p=0.006).

Systemic metastases at 3-year follow up

- TaTME=16.4%
- Laparoscopic TME=19.8%, HR=0.93 (95% CI 0.7 to 1.24, p=0.615)

Disease-free survival rates at 3-year follow up

- TaTME=74.3%
- Laparoscopic TME=68.6%. HR=0.81 (95% CI 0.65 to 1.02, p=0.078)

For patients who had TaTME with sphincter preservation, HR=0.78 (95% CI 0.62 to 0.98, p=0.033).

Overall survival at 3-year follow up

- TaTME=87.2%
- Laparoscopic TME=82.2%, HR=0.74 (95% CI 0.53 to 1.03, p=0.076)

For patients who had TaTME with sphincter preservation, HR=0.73 (95% CI 0.52 to 1.02, p=0.068).

Key safety findings

30-day postoperative complications

- TaTME=31.9%
- Laparoscopic TME=35.2%, p=0.382

Study 7 Caycedo-Marulanda A (2021)

Study details

Study type	Cohort study
Country	Canada (8 centres)
Recruitment period	2014 to 2018
Study population and number	n=608 Patients with rectal cancer
Age and sex	Median 63 years (IQR 54 to 70); 70% (423/608) male
Patient selection criteria	No defined patient selection criteria. All consecutive patients with primary rectal cancer treated by TaTME at 8 high-volume rectal cancer academic institutions across Canada were included.
Technique	Sequential or simultaneous approaches involving 1 or 2 surgical teams respectively were used depending on the institution and surgeon equipoise. Six centres always used a flexible platform for transanal minimally invasive surgery (Gel POINT path, Applied Medical), 1 centre exclusively used a rigid transanal endoscopy microsurgery system (Richard Wolf GmbH) and 1 site had access to both devices. Most surgeons used the procedure for tumours in the middle and lower third of the rectum, avoiding T4 lesions or those needing abdominoperineal resections. 92% of patients had a low anterior resection, 7% had an abdominoperineal resection and 1% had another form of resection. 61% of patients had a stapled anastomosis, 29% had a handsewn reconstruction and 9% had no anastomosis. Of those who had reconstruction, 86% had a diverting ileostomy. 70% of patients had neoadjuvant chemotherapy or radiotherapy.
Follow up	median 27 months (IQR 18 to 38)
Conflict of interest/source of funding	3 authors received grants or personal fees outside the submitted work from companies including Ethicon, CONMED, Southmedic, Johnson & Johnson, Stryker and Medtronic.

Analysis

Study design issues: Retrospective multicentre cohort study including all consecutive patients with primary rectal cancer treated by TaTME. The main outcome was the incidence of local recurrence. The cumulative probability of local recurrence- and systemic recurrence-free survival at 36 months was estimated. These were defined as radiologic or endoscopic evidence of 1 or more new lesions in or outside the pelvis, respectively, documented during surveillance after the removal of the primary tumour.

Study population issues: At baseline, the median body mass index was 27.0 kg/m^2 (IQR 24.1 to 31.3). The median tumour height was 6 cm (IQR 4 to 8) and 42% of patients had clinical stage 3 disease, 27% had stage 2 disease, 22% had stage 1 disease and 6% had stage 4 disease.

Key efficacy findings

Number of patients analysed: 608

Local recurrence

- Local recurrence rate=3.6% (22/608); 15 patients also had systemic recurrence.
- Median time to local recurrence=13 months (IQR 9 to 19 months)
- Probability of local recurrence-free survival at 24 months=97% (95% CI 95 to 99)
- Probability of local recurrence-free survival at 36 months=96% (95% CI 94 to 98)

Of the 22 patients with local recurrence, 16 (72.7%) were male, 14 (63.6%) had neoadjuvant chemoradiation, 12 (54.5%) had stage 3 disease, 16 (72.7%) had negative circumferential margin, 20 (90.9%) had a negative DRM and 2 (9.1%) had conversion to open surgery.

According to the Cox proportional hazards regression model, the hazard of local recurrence was estimated to be 4.19 (95% CI 2.86 to 6.15) times higher among patients with a positive CRM compared with those with a negative CRM.

Systemic recurrence

- Systemic recurrence rate=9.4% (57/608)
- Probability of systemic recurrence-free survival at 36 months=92% (95% CI 89 to 94)

In a multivariable model including disease stage, neoadjuvant therapy, CRM and DRM, only a positive CRM remained statistically significantly associated with systemic recurrence (adjusted HR 2.95, 95% CI 1.26 to 6.91).

Disease-free survival

- Probability of disease-free survival at 24 months=91% (95% CI 89 to 94)
- Probability of disease-free survival at 36 months=88% (95% CI 85 to 92)
- Probability of disease-free survival at 48 months=85% (95% 80 to 90)

Key safety findings

- Conversion rate=4.3% (26/608)
- Intraoperative complications=4.9% (30/608)
- Postoperative complications=55.8% (339/608)
- Clavien-Dindo grade 3 complications=14.5% (88/608)
- Clavien-Dindo grade 4 complications=0.8% (5/608)

Complications that appeared to be associated with transanal portion:

- Urethral injury=0.3% (2/608)
- Vaginal injury=0.2% (1/608)
- Defects made in rectum=0.5% (3/608); 1 patient subsequently had a local recurrence
- Presacral bleeding=1.0% (6/608); data did not capture whether these happened during the laparoscopic or transanal portion of the dissection

- Anastomotic leak rate within 30 days=7.6% (46/608)
- Readmission=16.4% (100/608)
- 30-day mortality=0.7% (4/608); 1 patient had a fatal stroke on postoperative day 4, 1 had an anastomotic leak and abscess and died on postoperative day 17 and 1 patient died of unknown causes on postoperative day 28. The fourth patient was presumed to have a perforated viscus on postoperative day 17; they had rapid decompensation and died.

Study 8 Yao H (2021)

Study details

Study type	Registry
Country	China (40 centres)
Recruitment period	2010 to 2019
Study population and number	n=1,283 (1,150 with rectal cancer) Patients who had TaTME for malignant or benign disease
Age	Median 61 years; 69% (888/1,283) male
Patient selection criteria	Patients who had laparoscopic-assisted TaTME for malignant or benign disease were included. Patients who had the transanal approach alone (taTME without abdominal assistance) were excluded.
Technique	Laparoscopic-assisted TaTME. Among 849 patients with rectal cancer who had taTME, 781 (94%) had anterior resection (21%) or low anterior resection procedures (73%). A 2-team approach was used in 43% (341/794) of patients with rectal cancer. A stapler was used in 612 patients (79%), and a handsewn reinforcement was also used after the stapled anastomosis in 71 patients (9%). The splenic flexure was mobilized in 207 patients (25%). The rate of defunctioning stoma application was 61%.
Follow up	to hospital discharge
Conflict of interest/source of funding	No financial disclosures were reported.

Analysis

Follow-up issues: Overall, 11% of data were missing. For some of the analysed variables, up to 35% of the data were missing.

Study design issues: Observational multicentre study using data from an online registry system (the Chinese Transanal Total Mesorectal Excision Registry Collaborative). The key outcomes measured were postoperative complications and pathological outcomes. For centres that participated in a training course, patient data were compared before and after the training date. Positive CRM was defined as the presence of tumour cells within 1 mm from the excised nonperitoneal surface of the rectum. Positive DRM was defined as the presence of tumour cells within 1 mm from the excised distal end of the specimen.

Study population issues: At baseline, patients had a median BMI of 23.6 kg/m^2 (range 14.5 to 46.3). The median distance from tumour lower edge to anal verge was 50 mm (range 0 to 180). It was reported that 36% of patients had neoadjuvant therapy.

Other issues: Among 40 participating centres, the average number of registered cases was 32, and 12 centres (30%) registered more than 40 cases in the registry.

Key efficacy findings

- Number of patients analysed: 1,283

Histopathological results in patients with rectal cancer who had laparoscopic assisted TaTME

Outcome	Total (n=849)
Pathological T stage, n (%)	
T0	39 (4.9)
T1	71 (9.0)
T2	241 (30.5)
T3	343 (43.4)
T4	96 (12.2)
Missing	59 (6.9)
Pathological N stage, n (%)	
N0	516 (64.2)
N1	207 (25.7)
N2	81 (10.1)
Missing	45 (5.3)
Quality of TME specimen, n (%)	
Complete	645 (81.9)
Near complete	144 (18.0)
Incomplete	1 (0.1)
Missing	50 (5.9)
Vessel or lymphatic invasion	
Positive	174 (23.2)
Negative	576 (67.8)
Missing	99 (11.7)
CRM, n (%)	
Positive	22 (2.8)
Negative	753 (95.8)
Not evaluated	11 (1.4)
Missing	63 (7.4)
Rectal tube perforation, n (%); 84 missing	8 (1.0)
Number of lymph nodes harvested, median (range); 49 missing	14 (0 to 51)
Maximum tumour size, mm, median (range); 108 missing	30 (0 to 115)
DRM, mm	
Median (range)	20 (0 to 202)
Positive DRM, n (%)	6 (0.7)
Missing, n (%)	192 (22.6)

Median length of postoperative stay=9 days (range 1 to 125); data missing for 42 (5%) patients

Key safety findings

The conversion rate was 0.5% in the abdominal phase and 1.9% in the perineal phase.

Intraoperative adverse events, n (%); data were missing for 301 (36%) patients

Event	Total (n=548)
Urethral injury	3 (0.5)
Pursestring failure	30 (5.5)
Incorrect dissection plane	46 (8.4)
Bleeding	70 (12.8)

Postoperative complications, n (%)

Outcome	Total (n=849)
Postoperative morbidity at discharge date (n=817)	150 (18.4)
Clavien-Dindo classification at discharge	
1	27 (3.2)
2	63 (7.4)
3	24 (2.8)
4 or 5	0 (0)
missing	68 (8.0)
Anastomotic leak at discharge date (among 796 patients who had primary anastomosis)	
Yes	44 (5.8)
No	710 (94.2)
missing	42 (5.3)
Grade of anastomotic leak	
Needing no active therapeutic intervention	9 (1.2)
Needing active therapeutic intervention but no relaparotomy	18 (2.4)
Needing relaparotomy	16 (2.1)
Missing	1 (0.1)
Pelvic abscess (n=817)	3 (0.4)

Study 9 Roodbeen S (2020)

Study details

Study type	Cohort study
Country	The Netherlands, Italy, France, Belgium and US
Recruitment period	2011 to 2018
Study population and number	n=767 Patients with mid- or low rectal cancer
Age	Median 64 years; 72% (552/767) male
Patient selection criteria	Patients with primary rectal adenocarcinoma were included. Selection criteria for TaTME in the individual institutions were as follows: 4 centres offered TaTME to all patients with mid- or low rectal cancer, 1 centre selected all low rectal cancers and males with a mid-rectal tumour for TaTME, and 1 centre initially started with TaTME for obese and distal tumours, gradually expanding their selection criteria to all mid- and low rectal cancers. Patients with benign disease, malignancies other than adenocarcinoma and recurrent tumours, as well as exenterative procedures were excluded.
Technique	After the insertion of the Gelpoint path, the lumen of the rectum was closed below the tumour by an airtight purse string. The rectum was then washed with betadine extensively before starting the full-thickness rectotomy. The purse string and rectotomy was done through an open or transanal minimal invasive surgery approach according to surgeon preference. For ultra-low cancers, the procedure started with an open or endoscopic rectotomy through a transanal minimally invasive approach followed by stump closure. Most of the TaTME procedures were low anterior resections (n=659; 86%) and 65% of patients had a stapled anastomosis (65%). The abdominal part of the TaTME procedure was completed laparoscopically in nearly all patients.
Follow up	Median 25.5 months (IQR 15 to 39)
Conflict of interest/source of funding	None

Analysis

Follow-up issues: Missing data did not exceed 15% for any variable.

Study design issues: Multicentre observational cohort study, including all consecutive patients with primary rectal adenocarcinoma who had TaTME in 6 tertiary referral centres. The primary endpoint was actuarial cumulative 2-year local recurrence rate (Kaplan -Meier survival analysis). Data were collected from either the prospective TaTME International registry or from the individual centres' prospective databases. Local recurrence specific data, which were not captured on these registries, were retrospectively collected on a study-specific case record form. An intention-to-treat analysis was done.

Study population issues: 150 (20%) patients were obese (body mass index 30 or above). The tumour was located within 1 cm of the anorectal junction in 213 (28%) patients. Median tumour height from the anorectal

junction was 3.0 cm (IQR 1.0 to 5.0). More than half of the patients (n=439; 58%) had an anterior tumour location. The mesorectal fascia was threatened in 273 (41%) patients. Presence of extramural vascular invasion on baseline MRI scans was reported in 143 (19%) patients and was scored as positive in 34 patients (24%). Most patients had neoadjuvant treatment (n=527; 69%).

Key efficacy findings

Number of patients analysed: 767

Histopathological outcomes

Outcome	n (%)
pT-stage – No residual tumour	116/767 (15.1)
T1	90/767 (11.7)
T2	150/767 (19.6)
T3	395/767 (51.5)
T4	8/767 (1.0)
Tx	8/767 (1.0)
pN stage	
N0	513/767 (66.9)
N1	177/767 (23.1)
N2	68/767 (8.9)
Nx	9/767 (1.2)
TME specimen	
Complete	607/753 (80.6)
Nearly complete	94/753 (12.5)
Incomplete	52/753 (6.9)
R1	62/767 (8.0)
Only DRM positive	6 (0.7)
Only CRM positive	48 (6.3)
DRM and CRM positive	8 (1.0)
Rectal perforation	8/766 (1.0)
Composite optimal pathology (CRM and DRM negative, complete or nearly complete TME specimen and no perforations)	647/752 (86.0)
Extramural vascular invasion	
Positive	78/132 (59.1)
Negative	54/132 (40.9)
Lymph nodes harvested, median (IQR)	16 (11 to 22)

Oncological outcomes

- After a median follow up of 25.5 months (IQR 15 to 39), local recurrence was identified in 24 (3.1%) patients.

- Local recurrence at 2 years, actuarial rate=3.3% (95% CI 1.9 to 4.8)
- Local recurrence at 3 years, actuarial rate=4.4% (95% CI 2.5 to 6.3)
- Time to local recurrence in months, median (IQR)=13.5 (8.3 to 21.8)
- Disease-free survival at 2 years, actuarial rate=81.6% (95% CI 78.5 to 84.7)
- Disease-free survival at 3 years, actuarial rate=77.6% (95% CI 73.9 to 81.2)
- Overall survival at 2 years, actuarial rate=95.3% (95% CI 93.6 to 97.0)
- Overall survival at 3 years, actuarial rate=93.4% (95% CI 91.2 to 95.7)

Location of local recurrence was lateral (n=10), posterior (n=8), and central (n=6). Four of the centrally located local recurrences were at the anastomotic site. No multifocal pattern of local recurrence was seen.

11 patients with local recurrence also had systemic disease progression, 3 of whom had palliative surgery and were still alive with disease at the time of data extraction. Eight had palliative chemotherapy, 3 of whom died during follow up and 5 were alive with disease at the time of data extraction.

Of the remaining 13 patients who had local recurrence only, 10 had salvage surgery, of whom 1 patient died because of new metastasis 5 months later; 1 patient was alive with disease (local and distant), and 8 were disease free at the end of follow up. Of the 3 patients who did not have salvage surgery, 1 patient had radiotherapy because of high sacral involvement and the other 2 patients were having chemotherapy at the time of data extraction with planned evaluation for resectability.

Four of the 24 patients with local recurrence died with disease, 12 were alive with disease and 8 were disease-free at the end of follow up.

Key safety findings

- Abdominal conversion rate to midline laparotomy=3%
- Perineal conversion=1% (11/767)
- Total morbidity within 30 days=39.9% (306/767)
- Major complications (Clavien–Dindo 3 or higher)=12.5% (96/767)
- Readmission within 30 days=8.0% (61/767)
- Clinically relevant intraoperative carbon dioxide embolism=0.3% (2/767)
- Urethral injury=0.3% (2/767)
- Postoperative death, n=1 (the patient died on postoperative day 3 because of sepsis related to colonic ischaemia)

Study 10 Denost Q (2018)

Study details

Study type	Randomised controlled trial
Country	France
Recruitment period	2008 to 2012
Study population and number	n=100 (50 TaTME, 50 laparoscopic) Patients with low rectal cancer
Age and sex	Median age 64 years (transanal), 63 years (laparoscopic); 69% (69/100) male
Patient selection criteria	Patients with a low rectal cancer (less than 6 cm from the anal verge) for whom sphincter-preserving surgery with handsewn coloanal anastomosis was suitable, were included. Exclusion criteria were patients with high and mid rectal cancers.
Technique	In the conventional laparoscopic group, a standard TME was done, to the top of the anal canal. In the transanal group, the abdominal component was only done after completion of the dissection from the perineal end. A retractor was used to expose the anal canal and a full thickness incision of the rectum was made, a minimum of 1 cm below the tumour. The rectal lumen was closed with a purse string suture and after lavage the dissection was done using standard instruments. After the transanal dissection of the distal rectum, a conventional laparoscopic procedure was done. In both groups, the specimen was extracted either through the anal canal or through a small suprapubic incision if the patient was obese or the specimen too bulky. A handsewn, side-to-end, or end-to-end, coloanal anastomosis was then done. All patients had a defunctioning loop ileostomy and these were reversed between the second and third postoperative month.
Follow up	Mean 5 years (range 1 to 92 months)
Conflict of interest/source of funding	None

Analysis

Follow-up issues: Follow-up visits were at 1 month, then every 4 months up to 2 years and then every 6 months. No patients were lost to follow up.

Study design issues: Single centre randomised controlled trial comparing TaTME with laparoscopic TME. Patients were blinded to their treatment allocation. Long-term oncologic outcomes were assessed, including local recurrence, overall- and disease-free survival. Local recurrence was defined as any recurrence diagnosed or suspected in the pelvis. Distant metastases were defined as any recurrence occurring outside of the pelvis. All recurrences were confirmed with radiological or histological examination. Overall and disease-free survival were measured from the date of surgery to death, recurrence and last follow-up evaluation.

Patients with M1 disease (synchronous metastases) were excluded from disease-free survival analysis. The study was not adequately powered to assess local recurrence.

The procedure description in the paper does not explicitly describe the use of an anal platform but the procedure is described as TaTME.

Study population issues: The 2 groups were balanced with respect to baseline characteristics and pathological staging. The number of patients who had adjuvant chemotherapy was 12 (24%) in the TaTME group and 19 (38%) in the laparoscopic group (p=0.130).

Data from this trial (reported in a different publication) are also included in the systematic review by Hajibandeh (2020).

Key efficacy findings

Number of patients analysed: 100 (50 TaTME, 50 laparoscopic TME)

Short term efficacy outcomes

Outcome	TaTME, n=50	Laparoscopic TME, n=50	p
Postoperative tumour stage pT0 to pT2, n (%)	30 (60)	28 (56)	0.685
Postoperative tumour stage pT3 to pT4, n (%)	20 (40)	22 (44)	-
Postoperative nodal stage pN0, n (%)	33 (66)	29 (58)	0.410
Postoperative nodal stage pN1 to pN2, n (%)	17 (34)	21 (42)	-
Analysed lymph nodes; median (range)	17 (2 to 30)	17 (9 to 40)	0.712
Distal margin (mm); median (range)	10 (0 to 30)	10 (1 to 30)	0.893
Positive distal margin, n (%)	1 (2)	4 (8)	0.362
Circumferential margin (mm); median (range)	7 (0 to 20)	5 (0 to 20)	0.833
R1 resection (positive CRM)	2 (4)	9 (18)	0.025
Quality of mesorectum – incomplete, n (%)	6 (12)	6 (12)	0.616
Quality of mesorectum – nearly complete, n (%)	9 (18)	13 (26)	-
Quality of mesorectum – complete, n (%)	35 (70)	31 (62)	-

Recurrences

5-year recurrence rate

- Overall=20.3% (95% CI 12.1 to 28.5)
- TaTME=15.5% (95% CI 4.9 to 26.1)
- Laparoscopic TME=25.1% (95% CI 12.8 to 37.4), p=0.129
- Mean time to recurrence was 21 months in the transanal group compared with 10 months in the laparoscopic group (p=0.351)

5-year local recurrence rate

- Overall=3.6% (95% CI 0.5 to 7.7)
- TaTME=2.6% (95% CI 2.3 to 7.5)
- Laparoscopic TME=4.8% (95% CI 1.7 to 11.3), p=0.300

The only independent predictive factor of the 5-year local recurrence was the R1 status (OR 12.69, 95% CI 1.77 to 91.11, p=0.012).

Survival

5-year overall survival

- TaTME=87.0% (95% CI 77.0 to 97.0)
- Laparoscopic TME=74.4% (95% CI 61.7 to 87.1), p=0.135

5-year disease-free survival

- TaTME=73.9% (95% CI 61.0 to 86.8)
- Laparoscopic TME=71.9% (95% CI 58.9 to 84.8), p=0.351

There were 2 independent predictive factors of both the 5-year overall and disease-free survival: the age of patients in overall survival (OR 5.10; 95% CI 1.69 to 15.37, p=0.004) and in disease-free survival (OR 3.00; 95% CI 1.34 to 6.65, p=0.007) and the R1 status in overall survival (OR 1.98; 95% CI 1.11 to 3.52, p=0.021) and in disease-free survival (OR 1.82; 95% CI 1.15 to 2.87, p = 0.010).

Key safety findings

Short term safety outcomes, n (%)

Outcome	TaTME, n=50	Laparoscopic TME, n=50	p
Conversion	2 (4)	5 (10)	0.436
Mortality	0	1 (2)	1.00
Overall morbidity	16 (32)	22 (44)	0.216
Surgical morbidity (Clavien Dindo 3 to 5)	6 (12)	7 (14)	0.766
Anastomotic leak or abscess	1 (2)	5 (10)	0.204
Occlusion	6 (12)	8 (16)	0.564
Reoperation	2 (4)	4 (8)	0.678
Urological morbidity	3 (6)	5 (10)	0.715

Study 11 Zeng Z (2020)

Study details

Study type	Randomised controlled trial (NCT02966483)
Country	China
Recruitment period	2016 to 2018
Study population and number	n=261 (128 TaTME, 133 laparoscopic TME) Patients with middle or lower rectal cancer
Age and sex	Mean 56 years; 66% (172/261) male
Patient selection criteria	Inclusion criteria included: histologically proven rectal adenocarcinoma, tumour located below the level of peritoneal reflection (determined by MRI), T3 to 4a, N0 or T1 to 4, N1-2 without threatened mesorectal fascia after treatment with neoadjuvant therapy. Exclusion criteria: inability to do sphincter preservation surgery, T4b tumour invading adjacent organs, neoadjuvant therapy indicated but patient unwilling to have it, recurrent cancer, concurrent or previous diagnosis of invasive cancer within 5 years, emergency surgery with intestinal obstruction or perforation, history of colorectal surgery, faecal incontinence, history of inflammatory bowel disease, and contraindications to surgery.
Technique	TaTME or laparoscopic TME For TaTME, 2 groups of surgeons operated simultaneously. A retractor system was used to sufficiently expose the anorectum to display the tumour. If the lower margin tumour was less than 5 cm from the anal margin, a semicircular anal speculum was used to expose the tumour. A purse string suture was placed to tightly occlude the rectal lumen and isolate the tumour. A port was introduced through the anus before insufflating with carbon dioxide. Conventional laparoscopic instruments were used for dissection. After delivering the specimen extracorporeally, an end to-end straight stapled anastomosis or handsewn anastomosis was done.
Follow up	Perioperative outcomes only
Conflict of interest/source of funding	None

Analysis

Study design issues: Data from patients who were enrolled in the randomised controlled trial and having treatment at the same hospital were included. Method of randomisation was not described. The aim of this analysis was to compare the pathological results of excision specimens and perioperative outcomes between TaTME and laparoscopic TME groups. The authors noted that this study may be underpowered. The main trial has an estimated sample size of 1,114 patients and is scheduled to be completed in July 2025, with the primary endpoint being 3-year survival.

The procedure description in the paper does not explicitly describe the use of an anal platform but the procedure is described as TaTME.

Study population issues: The baseline characteristics of the 2 groups were similar. The mean body mass index was 22.5 kg/m^2 (range 17.0 to 33.2) in the transanal group and 22.2 kg/m^2 (range 14.2 to 31.6) in the laparoscopic group.

Key efficacy findings

Number of patients analysed: 261 (128 TaTME, 133 laparoscopic TME)

Pathological results

Outcome	TaTME	Laparoscopic TME	p
Mesorectal resection quality, n (%)			0.173
Complete	121 (94.5)	119 (89.5)	-
Nearly complete	7 (5.5)	14 (10.5)	-
Incomplete	0 (0)	0 (0)	-
Evaluated lymph nodes, median (range)	15 (2 to 35)	16 (0 to 66)	0.069
DRM status – positive	0 (0)	2 (1.5)	0.498
DRM status – negative	128 (100)	131 (98.5)	-
CRM status – positive	2 (1.6)	2 (1.5)	0.674
CRM status – negative	126 (98.4)	131 (98.5)	-
Postoperative T stage, n (%)			0.542
Tis and T0	8 (6.3)	7 (5.3)	-
T1	11 (8.6)	13 (9.8)	-
T2	36 (28.1)	49 (36.8)	-
T3	70 (54.7)	60 (45.1)	-
T4	3 (2.3)	4 (3.0)	-
Postoperative N stage, n (%)			0.424
N0	81 (63.3)	94 (70.7)	-
N1	34 (26.6)	27 (20.3)	-
N2	13 (10.1)	12 (9.0%)	-

Key safety findings

Perioperative outcomes

Outcome	TaTME	Laparoscopic TME	p
Operation time in minutes, mean (standard deviation); range	213.2 (58.9); 70 to 373	235.3 (82.0); 62 to 540	0.044
Intraoperative blood loss (ml), mean (standard deviation); range	69.4 (53.9); 10 to 500	79.2 (66.3); 5 to 400	0.374
Preventive ileostomy, n (%)	69 (53.9%)	93 (69.9%)	0.008
Conversion	0 (0%)	0 (0%)	1.00
Complication, n (%)	13 (10.2%)	19 (14.3%)	0.309
Anastomotic leakage	7 (5.5%)	5 (3.8%)	-
Obstruction	3 (2.3%)	9 (6.8%)	-
Anastomotic stenosis	1 (0.8%)	1 (0.7%)	-
Uroschesis	1 (0.8%)	1 (0.7%)	-
Incisional hernia	0 (0%)	2 (1.5%)	-
Bleeding	0 (0%)	1 (0.7%)	-
Peritonitis	1 (0.8%)	0 (0%)	-
Secondary operation because of complication, n (%)	2/13 (15.3%)	7/19 (36.8%)	0.353
30-day mortality	0	0	1.00

Study 12 Ren J (2021)

Study details

Study type	Randomised controlled trial
Country	China
Recruitment period	2017 to 2019
Study population and number	n=64 (32 TaTME, 32 laparoscopic TME) Patients with low rectal cancer
Age and sex	Mean age 66 years (transanal), 67 years (laparoscopic); 58% (37/64) male
Patient selection criteria	Inclusion criteria: rectal adenocarcinoma, the distance of the tumour from the anal verge was less than 7 cm, the tumour diameter was less than 5 cm, preoperative clinical stage 1 to 3 and preoperative anaesthesia grade 1 to 3. Exclusion criteria: tumour invaded adjacent organs or distant metastases, acute intestinal obstruction, multiple primary colorectal cancer, Miles surgery or Hartmann surgery.
Technique	TaTME or laparoscopic TME An operating platform (not further described) was used for TaTME. Neoadjuvant chemoradiotherapy was recommended for patients with clinical stage T3 or N+ tumours.
Follow up	To discharge
Conflict of interest/source of funding	None

Analysis

Follow-up issues: Patients were only followed up to hospital discharge.

Study design issues: Single centre randomised controlled trial, comparing TaTME with laparoscopic TME. The method of randomisation was described as a 'random number method'. Patients with an even number were assigned to the laparoscopic group and odd numbers to the transanal group. The final sample size of 64 was calculated based on the assumption that the procedures were equivalent for CRM distance.

Study population issues: There were no statistically significant differences between the groups for baseline characteristics, including gender, age, body mass index, preoperative comorbidities (coronary heart disease, chronic bronchial emphysema, chronic renal insufficiency), preoperative American Society of Anesthesiologists score, tumour distance from the anal verge, tumour size, neoadjuvant therapy, clinical T stage, clinical N stage and protective ileostomy. Of the 64 patients, 69% had neoadjuvant chemotherapy; 4 patients in the TaTME group and 5 patients in the laparoscopic TME group were offered it but declined.

Key efficacy findings

Number of patients analysed: 64 (32 TaTME, 32 laparoscopic TME)

Pathological results

Outcome	TaTME group	laparoscopic group	p
Harvested lymph nodes, mean (standard deviation)	19.50 (6.54)	21.06 (5.94)	0.321
Mesorectum integrity, n			0.329
Complete	26	21	-
Nearly complete	5	8	-
Incomplete	1	3	-
CRM involvement (yes/no)	1/31	4/28	0.355
CRM distance (mm)	6.81 (2.99)	5.22 (3.05)	0.039
DRM involvement (yes/no)	0/32	2/30	0.492
R1 resection (yes/no)	1/31	6/26	0.104
Complete remission (yes/no)	2/30	3/29	1.00
Pathological T stage, n			0.961
T1	4	4	-
T2	11	12	-
T3	14	13	-
Pathological N stage, n			0.852
N0	22	24	-
N1	6	5	-
N2	4	3	-
Pathological TNM stage, n			0.738
1	11	12	-
2	9	10	-
3	10	7	-

Key safety findings

Perioperative outcomes

Outcome	TaTME group	laparoscopic group	p
Operative time in minutes, mean (standard deviation)	212.59 (28.71)	187.66 (27.15)	0.001
Conversion (yes/no)	0/32	2/30	0.492
Intraoperative complication (yes/no)	2/30	1/31	1.00
Morbidity (yes/no)	6/26	5/27	0.740
Severe morbidity (yes/no)	2/30	3/29	1.00
Anastomotic leak (yes/no)	2/30	3/29	1.00
Unplanned reoperation (yes/no)	1/31	1/31	1.00
Hospital stay in days, mean (standard deviation)	11.31 (2.97)	11.56 (4.56)	0.796

The severe complications in the TaTME group were intra-abdominal bleeding (n=1) and acute heart failure (n=1). In the laparoscopic group, they were anastomotic bleeding (n=1), anastomotic leak (n=1) and acute renal failure (n=1).

Study 13 Dickson E (2019)

Study details

Study type	Case series from registry data
Country	International
Recruitment period	2015 to 2018
Study population and number	n=25 Patients who had carbon dioxide embolism after TaTME
Age	Mean 60 years; 76% (19/25) male
Patient selection criteria	Patients who had carbon dioxide embolism after TaTME were included.
Technique	Of the 20 patients with cancer, 16 had anterior resections with or without a stoma, 3 had abdominoperineal resection and 1 had mesorectal excision. A flexible transanal platform was used in all patients. Synchronous abdominal and transanal operating was done in 60% (15/25) of patients. Although none of the cases used transoesophageal echocardiography for routine monitoring, 32% of reports described its use to confirm multiple gas emboli during a suspected event.
Follow up	Not reported
Conflict of interest/source of funding	One author has received consulting, teaching, and speaking fees for Conmed Ltd, Applied Medical, and Stryker.

Analysis

Study design issues: Retrospective study done at the collaborating centres from the international TaTME registries (the LOREC and OSTRiCh TaTME registries). The authors e-mailed all collaborators with repeated reminders to verify and confirm data entered and to obtain as much information as possible about the cases. The authors noted that some cases of carbon dioxide embolism may not have been recognised as such, so the true incidence may be higher.

Study population issues: Of the 25 patients, 20 (80%) had TaTME for cancer. The median tumour height from the anorectal junction on MRI was 4 cm (range 0 to 12).

Key safety findings

The incidence of clinically apparent carbon dioxide embolism during TaTME was estimated to be about 0.4% (25/6,375).

A fall in end tidal carbon dioxide was noted as the initial feature in 22 patients, with 13 (52%) developing signs of hemodynamic compromise. All of the events occurred in the transanal component of dissection, with mean

(range) insufflation pressures of 15 mmHg (12 to 20 mmHg). Patients were predominantly (68%) in a Trendelenburg position, between 30° and 45°.Venous bleeding was reported in 20 patients at the time of carbon dioxide embolus, with periprostatic veins documented as the most common site (40%). After carbon dioxide embolus, 84% of procedures were completed after hemodynamic stabilisation. A conversion to open surgery occurred in 7 patients (28%), and 13 procedures (52%) were switched from a transanal approach to a top-down laparoscopic approach. A restorative procedure was changed to a Hartmann procedure in 2 patients.

Two patients needed cardiopulmonary resuscitation because of cardiovascular collapse. There were no deaths.

Unplanned admission to the intensive care unit or high dependency unit was necessary in 15 patients (60%) after surgery.

Study 14 Perdawood S (2018)

Study details

Study type	Case report
Country	Denmark
Recruitment period	Not reported
Study population and number	n=1 Patient with soft tissue metastasis in the perianal region after TaTME for rectal cancer.
Age and sex	82-year-old man
Patient selection criteria	Not applicable
Technique	Hybrid laparoscopic-transanal procedure, starting with the abdominal part. The transanal part began with fixation of a retractor to the skin around the anus. The Gel POINT access platform (Applied Medical, USA) was used and after intraluminal rectal washout with water and antiseptic solution, a purse-string suture was made 1 cm under the tumour. The purse-string suture stayed intact throughout the procedure. A full-thickness incision of the rectal wall was made 1 cm under the suture and a “bottom-up” TME was completed. After making a purse-string suture on the rectal stump, the specimen was removed through the anus, without using a wound protector. After bowel transection, a side-to-end anastomosis was made with a circular stapler and a loop ileostomy was created. The anastomosis was intact. The procedure was number 38 for the author in the learning curve of consecutive TaTME procedures.
Follow up	19 months
Conflict of interest/source of funding	None

Key safety findings

Case report – possible port-site metastasis

The patient had a TaTME procedure for a rectal tumour that was classified as T3, located mainly anteriorly, 7 cm from the anal verge and 6 mm from the mesorectal fascia. The pathologist reported a complete mesorectal specimen with no defects and a stage of T3N2. The CRMs and DRMs were not involved. Seven out of 19 retrieved lymph nodes were positive. The patient had adjuvant chemotherapy and then ileostomy closure 10 months after the TaTME procedure.

19 months after the TaTME, the patient presented with a mass in the perianal region, which was locally excised under general anaesthesia. Histopathological examination showed adenocarcinoma representing a local recurrence that was not removed completely. The morphological characteristics were identical to the primary tumour. The lower part of the rectum and anal canal were treated with neoadjuvant chemoradiation before an abdominoperineal excision.

The author stated that a possible mechanism could be direct implantation to the small wounds at the sites of inserted sharp hooks of the retractor. The definitive mechanism of recurrence could not be established. The author concluded that this case report demonstrates that even with rectal washout and an intact purse-string suture there is a risk of implantation metastasis.

Study 15 Balaphas A (2018)

Study details

Study type	Case reports
Country	Switzerland
Recruitment period	Not reported
Study population and number	n=4 Patients with colonic conduit prolapse after TaTME for low rectal cancer
Age and sex	Ages 60, 65, 66 and 76 years; 100% (4/4) male
Patient selection criteria	Not applicable
Technique	Of the 4 patients, 2 had a total intersphincteric resection, 1 had a partial intersphincteric resection and 1 had a subtotal intersphincteric resection. All anastomoses were handsewn and protected with an ileostomy.
Follow up	282, 422, 606, and 1019 days
Conflict of interest/source of funding	None

Key safety findings

Case reports – colonic conduit prolapse

Colonic conduit prolapse was seen 44, 79, 243, and 958 days after TaTME. Three patients had transanal repair with colonic resection, new hand-sewn anastomosis and levatorplasty and 1 patient had an additional overlapping sphincteroplasty as part of the procedure. Two patients had 2 recurrences of prolapse which were managed by the same technique as primary repair. In 1 patient, a biological mesh was added to retain the posterior colonic conduit in the pelvis. The same patient developed a posterior ectropion of rectal mucosa. This was managed by semi-circular resection of the anastomosis, post-anal repair, reanastomosis, and Sarafoff incision. The patient then had a third recurrence and was awaiting surgery at the time of report.

Study 16 Alimova I (2021)

Study details

Study type	Systematic review
Country	Included studies were from the Netherlands, France, Taiwan, US, Poland, Denmark
Recruitment period	Search date: February 2020
Study population and number	n=638 patients (323 TaTME, 315 laparoscopic TME); 10 studies Patients with rectal cancer
Age and sex	TaTME: Mean age ranged from 58 to 68 years; 68% male Laparoscopic TME: Mean age ranged from 59 to 67 years; 62% male
Patient selection criteria	The following eligibility criteria were selected for inclusion of the publications in the meta-analysis: (a) population: patients were diagnosed with rectal cancer; (b) intervention: surgical treatment; (c) comparison: TaTME versus LaTME; (d) outcomes: long-term outcomes (locoregional recurrence, distant metastases, disease-free and overall survival), functional results and quality of life compared between 2 groups; and (e) study design: RCTs, cohort trials or matched case–control trials with sample size greater than 15. The exclusion criteria were as follows: (a) lack of the sufficient data or outcomes of interest; (b) duplicate publication; (c) abdominoperineal resections and (d) non-comparative studies, reviews, meta-analyses, letters, case reports or conference abstracts.
Technique	TaTME compared with laparoscopic TME.
Follow up	Mean follow up ranged from 13 to 32 months for TaTME and 25 to 75 months for laparoscopic TME.
Conflict of interest/source of funding	None

Analysis

Study design issues: The aim of the study was to compare long-term oncological, functional outcomes and quality of life after TaTME and laparoscopic total mesorectal excision for rectal cancer. The systematic review and meta-analysis were done in accordance with Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines. There were 8 matched case control studies, 1 prospective cohort study and 1 retrospective study. The quality of non-randomised controlled trials was evaluated using the Newcastle–Ottawa Scale criterion. The results ranged from 7 to 8 stars, which corresponded to good quality.

Study population issues: Most of the studies in this review were also included in the systematic review by Hajibandeh et al. (2020). The mean follow-up periods for oncological and functional outcomes were statistically significantly shorter for TaTME than laparoscopic TME.

Key efficacy findings

Number of patients analysed: 638 (323 TaTME, 315 laparoscopic TME)

Local recurrence rate (6 studies)

- TaTME=2.1%
- Laparoscopic TME=3.2%, OR 0.78 (95% CI 0.22 to 2.79, p=0.71; I^2=0%; n=405)

Distant metastasis rate (3 studies)

- TaTME=7.1%
- Laparoscopic TME=13.3%, OR 0.53 (95% CI 0.19 to 1.47, p=0.23; I^2=0%; n = 196)

2-year overall survival (3 studies)

- RR=1.04 (95% CI 0.97 to 1.11, p=0.25; I^2=27%; n=239)

2-year disease-free survival (3 studies)

- RR=1.01 (95% CI 0.92 to 1.11, p=0.86; I^2=0%; n = 239)

Mean LARS score (4 studies)

- The mean LARS score was statistically significantly higher in the TaTME group than in the LaTME group (Weighted MD 2.88; 95% CI 0.15 to 5.60; p=0.04; I^2=0%).

Mean Wexner score (2 studies)

- There was no statistically significant difference in the mean Wexner score between the 2 groups for (Weighted MD -0.79; 95% CI -3.00 to 1.42; p=0.48; I^2=34%)

Mean IPSS (2 studies)

- There was no statistically significant difference in the mean IPSS (Weighted MD -1.06; 95% CI -5.59 to 3.46; p=0.64; I^2=53%)

Key safety findings

Not reported

Study 17 An Y (2021)

Study details

Study type	Systematic review
Country	Included studies were from Egypt, Saudi Arabia, Denmark, France, Canada, China, US, Italy, the Netherlands, Belgium, Spain, Portugal, Lithuania, Korea, Germany, Poland, Russia, UK
Recruitment period	Search date: October 2019
Study population and number	n=2,446 patients (41 studies) Patients with rectal cancer
Age and sex	Pooled mean 63 years; 68% male
Patient selection criteria	All studies with at least 5 patients who had TaTME and complications were reported in the full text were included. In the case of overlapping cohorts, the studies with the largest cohorts were included. The following studies were excluded: reviews, meta-analyses, letters, case reports, editorials, expert opinions, conference abstracts, articles describing the surgical technique or videos, study protocols; nonhuman research; manuscripts not in the English language; patients with inflammatory bowel disease, familial adenomatous polyposis or hereditary nonpolyposis colorectal cancer; TaTME with a robotic transanal approach; TaTME without any abdominal approach; completion TaTME; TaTME without any kind of endoscopic pneumoperineal platform.
Technique	TaTME
Follow up	30-day morbidity was reported in 49% of studies (20/41) and morbidity at any time was reported in 42% (16/41 studies). One study reported 90-day morbidity.
Conflict of interest/source of funding	None

Analysis

Study design issues: The review was done according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines. The primary aim was to determine a pooled morbidity and anastomotic leakage rate after TaTME surgery, and the secondary aim was to show the completeness of reporting of complications among the included studies, as well as the correlation between completeness and reported incidence of complications. If a study only reported 30-day mortality or the 30-day readmission rate without clearly showing 30-day complication details, the complication results were not regarded as 30-day complication results. Methodological quality was assessed with the Methodological Index for Non-randomized Studies instrument. The median score was 10/16 (range 5 to 13). There were 14 comparative and 27 non-comparative studies.

Study population issues: The pooled mean height of the tumour from the anal verge was 5.8 cm (95% CI 5.2 to 6.3). Neoadjuvant therapy at baseline was reported for 57% (1360/2,404) of patients.

Key efficacy findings

Not reported

Key safety finding

Number of patients analysed: 2,446

Postoperative morbidity

- Pooled postoperative morbidity rate=30.0% (95% CI 26.4% to 34.0%; 37 studies; I^2=65%)
- Pooled rates of Clavien-Dindo grade 1 or 2 complications=19.5% (95% CI 16.0% to 23.6%; 26 studies)
- Pooled rates of Clavien-Dindo grade 3 or 4 complications=10.1% (95% CI 8.0% to 12.7%; 26 studies)
- Pooled 30-day mortality=0.4% (95% CI 0.1% to 1.4%; 30 studies).

Anastomotic leak

- Pooled anastomotic leakage rate=6.8% (95% CI 5.2% to 8.9%; 41 studies; I^2=17%)
- 4 studies reported late anastomotic leakage (diagnosed more than 30 days after the index surgery), including 4 asymptomatic cases diagnosed with CT scan 6 to 8 weeks after the index surgery, 2 asymptomatic cases diagnosed before ileostomy reversal and 13 cases diagnosed after postoperative day 30 without further interpretation.

Other complications

- Pelvic abscess, n=43 (15 studies)
- Rectovaginal fistulas, n=2; both treated surgically
- Vesicocolic fistula, n=1; treated surgically
- 8 ‘subclinical’ anastomotic fistulas were reported in 1 study.
- Anastomotic strictures, n=15
- Anastomotic sinus, n=1; managed conservatively

Sub-analysis (comparison of studies reporting 30-day results against those without a specified follow up time)

- Pooled morbidity rate in studies with 30-day results=35.5% (95% CI 31.8% to 39.4%; 20 studies)
- Pooled morbidity rate in studies without specified follow up = 23.4% (95% CI 17.8% to 30.1%; 16 studies), p=0.003

Study 18 Ose I (2021)

Study details

Study type	Non-randomised comparative study
Country	Denmark
Recruitment period	2014 to 2018
Study population and number	n=2,393 (312 TaTME, 1,163 laparoscopic TME, 205 open TME, 713 robotic TME) Patients with rectal cancer
Age and sex	Mean age 65.7 years (TaTME), 67.6 (laparoscopic TME), 67.0 (open TME), 67.3 (robotic TME), p=0.026 Male: 73% (227/312), 61% (714/1,164), 64% (132/205), 66% (473/713) respectively, p=0.001
Patient selection criteria	Inclusion criteria: rectal cancer, TME as the operation done, curative procedure and a 2014 to 2018 time interval. The procedures included low anterior resection, Hartmann's procedure and intersphincteric abdominoperineal excision. Rectal cancer was defined as an adenocarcinoma located at, or below, 15 cm from the anal verge. Patients who had extralevator APE and pelvic exenteration were excluded.
Technique	TaTME, laparoscopic TME, open TME, robotic TME
Follow up	30 days
Conflict of interest/source of funding	None

Analysis

Follow-up issues:

Study design issues: Data was extracted from the nationwide Danish Colorectal Cancer Group database, which is a population-based clinical colorectal cancer database with a 95% rate of data-completeness. Operating surgeons and pathologists report prospectively to the database and reporting is mandatory. The primary aim was to investigate the rates of non-radical resection (defined as an involved resection margin), and the secondary aim was to investigate the rate of anastomotic leakage within 30 days after surgery.

Study population issues: The mean tumour distance from the anal verge in the TaTME group was 7.85 cm and was statistically significantly lower compared to tumour height in the laparoscopic (8.67 cm) and robotic (8.70 cm) groups (p<0.001 for both). A larger number of patients in the open group had preoperative neoadjuvant radiotherapy (5.4%, 1.7%, 3.1%, and 1.0% for open, laparoscopic, robotic and TaTME groups, respectively), chemoradiation (29.7%, 13.9%, 17.3% and 16.3%, respectively), and chemotherapy (6.3%, 2.0%, 1.8% and 2.2%, respectively).

Other issues: TaTME was introduced in Denmark in 2013, so some of the centres were still in the early phase of the learning curve.

Key efficacy findings

Number of patients analysed: 2,393

Pathological outcomes

Outcome	TaTME, n=312	open TME, n=205	Laparoscopic TME, n=1,163	Robotic TME, n=713	p value
T stage, n (%)					
T0	7 (2.2)	7 (3.4)	30 (2.5)	22 (3.0)	0.001
T1	42 (13.4)	12 (5.8)	167 (14.3)	103 (14.4)	
T2	95 (30.4)	37 (18.0)	328 (28.2)	191 (26.7)	
T3	162 (51.9)	137 (66.8)	595 (51.1)	375 (52.5)	
T4	6 (1.9)	12 (5.8)	43 (3.6)	22 (3.0)	
N stage, n (%)					
N0	237 (75.9)	148 (72.1)	958 (82.3)	526 (73.7)	<0.001
N1	45 (14.4)	26 (12.6)	124 (10.6)	105 (14.7)	
N2	30 (9.6)	31 (15.1)	81 (6.9)	82 (11.5)	
Positive resection margin, n (%)	18 (5.7)	17 (8.2)	55 (4.7)	18 (2.5)	0.002

In multivariate analysis, the risk of positive resection margin was associated with having a T4 tumour and intraoperative bowel perforation (p<0.001 for both).

Key safety findings

Anastomotic leak

- TaTME=9.6%
- Open TME=11.6%
- Laparoscopic TME=11.5%
- Robotic TME=12.2%, p=0.698

The univariate analysis showed that male gender (OR 2.27; 95% CI: 1.5 to 3.2; p<0.001), high BMI (OR 1.58; 95% CI 1.0 to 2.4; p=0.037), high ASA score (OR 1.7; 95% CI 1.08 to 2.8; p=0.022) and intraoperative bowel perforation (OR 2.8; 95% CI 1.17 to 6.7; p=0.020) were independently associated factors with anastomotic leakage. In the multivariate model, gender (OR 2.27; 95% CI 1.5 to 3.3; p<0.001), perforation (OR 2.8; 95% CI 1.16 to 6.8; p=0.022) and BMI (OR 1.48; 95% CI 0.9 to 2.3; p=0.049) were associated factors with anastomotic leakage.

Intraoperative results

Outcome	TaTME, n=312	open TME, n=205	Laparoscopic TME, n=1,163	Robotic TME, n=713	p value
Conversion to open procedure, n (%)	4 (1.3)	-	127 (10.9)	40 (5.6)	<0.001

Bowel perforation, n (%)	9 (2.9)	16 (7.8)	43 (3.7)	34 (4.8)	0.028
Intraoperative vagina lesions, n (%)	4 (1.3)	2 (1.0)	(0.0)	0 (0.0)	<0.001
Intraoperative bladder lesions, n (%)	2 (0.6)	0 (0.0)	8 (0.7)	0 (0.0)	0.100
Intraoperative urethral lesions, n (%)	3 (1.0)	1 (0.5)	4 (0.34)	0 (0.0)	0.101
Intraoperative ureteric lesions, n (%)	3 (1.0)	2 (0.97)	4 (0.34)	0 (0.0)	0.056
Intraoperative lesions of presacral veins, n (%)	1 (0.32)	0 (0.00)	7 (0.60)	0 (0.0)	<0.001
Blood loss, mean (SD), ml	101.4 (236.2)	526.6 (796.9)	168.9 (356.6)	128.8 (180.8)	<0.001

Postoperative surgical complications

Outcome	TaTME, n=312	open TME, n=205	Laparoscopic TME, n=1,163	Robotic TME, n=713	p value
Surgical complications, n (%)	77 (24.7)	55 (26.8)	300 (25.8)	192 (26.9)	0.875
Bleeding, n (%)					
Clavien-Dindo 1 or 2	0	2 (1.0)	7 (0.6)	10 (1.4)	0.165
Clavien-Dindo 3	2 (0.6)	0	14 (1.2)	8 (1.1)	
Clavien-Dindo 4	1 (0.3)	0	1 (0.1)	0	
Clavien-Dindo 5	0	0	4 (0.4)	0	
Wound dehiscence, n (%)					
Clavien-Dindo 1 or 2	0	1 (0.5)	1 (0.1)	1 (0.1)	0.129
Clavien-Dindo 3	0	7 (3.4)	14 (1.2)	8 (1.1)	
Clavien-Dindo 4	0	1 (0.5)	2 (0.2)	0	
Clavien-Dindo 5	0	0	1 (0.1)	0	
Bowel obstruction, n (%)					
Clavien-Dindo 1 or 2	9 (2.9)	10 (4.9)	37 (3.2)	24 (3.3)	0.125
Clavien-Dindo 3	12 (3.8)	4 (2.0)	29 (2.5)	17 (2.4)	
Clavien-Dindo 4	0	0	3 (0.3)	2 (0.2)	
Clavien-Dindo 5	0	0	1 (0.1)	0	
Wound infection, n (%)					
Clavien-Dindo 1 or 2	5 (1.6)	4 (2.0)	15 (1.3)	8 (1.1)	0.429
Clavien-Dindo 3	7 (2.3)	8 (3.9)	23 (2.0)	12 (1.7)	
Clavien-Dindo 4	0	0	4 (0.4)	0	
Intra-abdominal abscess, n (%)					
Clavien-Dindo 1 or 2	0	1 (0.5)	7 (0.6)	3 (0.4)	0.086
Clavien-Dindo 3	6 (2.0)	10 (4.9)	22 (1.8)	20 (2.8)	
Clavien-Dindo 4	0	1 (0.5)	2 (0.2)	3 (0.4)	
Clavien-Dindo 5	0	0	1 (0.1)	0	

Stoma complications, n (%)					
Clavien-Dindo 1 or 2	11 (3.6)	2 (1.0)	12 (1.0)	14 (2.0)	0.074
Clavien-Dindo 3	10 (3.2)	3 (1.5)	35 (3.0)	22 (3.1)	
Clavien-Dindo 4	0	1 (0.5)	3 (0.3)	2 (0.3)	
Clavien-Dindo 5	0	0	1 (0.1)	2 (0.3)	
30-day mortality	3 (1.0)	0	21 (1.8)	6 (0.8)	0.029

Study 19 Van Oostendorp S (2021)

Study details

Study type	Cohort study
Country	The Netherlands (6 centres)
Recruitment period	2012 to 2020
Study population and number	n=624 Patients with primary rectal cancer
Age and sex	mean 66 years; 71% (440/624) male
Patient selection criteria	All consecutive cases of TaTME for primary rectal cancer since the start of this technique in each of the 6 centres were included.
Technique	TaTME A low anterior TME resection was done in 539 patients (86%). In these a primary anastomosis was constructed without diversion in 103 (17%), anastomosis with a diverting ileostomy in 337 (54%) and nonrestorative end-colostomy (Hartmann) in 99 patients (16%). An intersphincteric resection with creation of an end-colostomy was done in 80 patients (13%) and a TaTME resection as part of a proctocolectomy was done in 5 patients.
Follow up	Mean 29 months, median 27 months (range 1 to 82 months).
Conflict of interest/source of funding	None

Analysis

Study design issues: Prospective, multicentre cohort study. The main aim was to assess the local recurrence rate during the initial implementation, continued adoption and prolonged experience of TaTME in 6 hospitals in the Netherlands.

Study population issues: The caseload among the 6 participating centres ranged between 47 and 227. The 3 cohorts defined as the initial implementation (cases 1 to 10), continued adoption (cases 11 to 40) and prolonged experience (case 41 onward) constituted 60, 180 and 384 patients, respectively. Of the 624 patients, 9% was classified as obese (BMI 30kg/m^2 or above). Almost half of all tumours (46%) were located below or within 3 cm of the anorectal junction. Clinical tumour staging showed cT4 in 6% and cT3 in 67%. The mesorectal fascia was threatened in 154 (25%) patients, of whom 68 showed a persistent threatened margin upon restaging after neoadjuvant treatment. Synchronous distant metastases were present in 47 patients (8%); these were mostly hepatic followed by a pulmonary location.

Key efficacy findings

Number of patients analysed: 624

Local recurrence

- Local recurrence rate=4.8% (30/624) after a median interval of 17 months (range 5 to 61 months) from index surgery.
- The predominant location for recurrence was presacral (n=16; 53%) while a multifocal pattern was seen in 6 local recurrences.
- Kaplan–Meier survival analysis showed an estimated local recurrence rate in the total study population of 4.6% at 2 years and 6.6% at 3 years.
- Comparative analyses of the 3 predefined cohorts showed a 3-year local recurrence rate of 14.0% in the initial implementation, 5.3% during continued adoption and 5.9% with prolonged experience (p=0.036).
- Exclusion of patients with a persistent threatened margin after neoadjuvant therapy showed a Kaplan–Meier estimated local recurrence rate of 3.7% at 2 years and 5.6% at 3 years.
- Cox proportional hazard regression analysis to identify predictive risk factors for local recurrence revealed experience to be a consistent independent predicting factor in uni-and multivariate analysis next to a persistent threatened margin to the mesorectal fascia following neoadjuvant therapy, advanced stage pT3-4, presence of pathological lymph nodes and pelvic sepsis.
- Adjusted Cox regression analysis to correct for case mix projected the 3-year local recurrence rate to be 9.6%, 2.9% and 3.1% for the 3 cohorts, respectively. Both the continued adoption phase (HR 0.290, 95% CI 0.108 to 0.780, p=0.014) and prolonged experience (HR 0.318, 95% CI 0.127 to 0.795, p=0.014) had a statistically significant lower hazard of developing a local recurrence compared with the initial implementation cohort.

Key safety findings

Conversion

- No conversion, n=595 (95.4%)
- Laparotomy, n=15 (2.4%)
- Pfannenstiel, n=5 (0.8%)
- Laparoscopy, n=7 (1.1%)
- Open abdominoperineal resection, n=1 (0.2%)

Intraoperative complications

- Urethral injury, n=1 (0.2%)
- CO_2 embolus, n=5 (0.8%)
- Pelvic bleeding, n=11 (1.8%)
- Visceral injury, n=7 (1.1%)
- Purse-string failure, n=14 (2.2%)
- Rectal perforation, n=21 (3.4%)
- Anastomotic problem, n=62 (10.0%)
- Technical problem transanal phase, n=3 (0.5%)

Postoperative complications (30 day)

- None, n=289 (46.3%)
- Clavien-Dindo 1, n=57 (9.1%)
- Clavien-Dindo 2, n=120 (19.2%)
- Clavien-Dindo 3a, n=24 (3.8%)
- Clavien-Dindo 3b, n=93 (14.9%)
- Clavien-Dindo 4, n=36 (5.8%)
- Clavien-Dindo 5, n=5 (0.8%)

Major surgical morbidity (30 day)

- Clavien-Dindo class 3 or above, n=149 (23.9%)

Short-term leakage or abscess (30 day)

- Anastomosis (n=443), n=89 (20.1%)
- Non-restorative (n=181), n=31 (17.1%)

Overall pelvic sepsis

- Early or late leakages, abscess or sinus=140 (22.4%)

Anastomotic takedown

- Unintended take down of anastomosis and creation of end colostomy because of septic complications, n=42 (9.5%)

Validity and generalisability of the studies

- Three randomised controlled trials were identified, all of which compared TaTME with laparoscopic TME. In 2 of these trials, the procedure description does not mention use of an anal platform (Denost 2018; Zeng 2020).
- One of the randomised controlled trials reported preliminary data on perioperative outcomes before the main trial had completed recruitment (Zeng 2020).
- There is heterogeneity among studies with respect to the surgical procedure and the type of platform and instruments used.
- Most of the studies report early experience of using the procedure.
- There may be differences between studies in the identification and reporting of adverse events.
- Although there is a lack of longer term outcomes, several studies report follow up beyond 2 years. One randomised controlled trial has a mean follow up of 5 years.
- The studies include data from Europe (including the UK), North America and Asia.
- There is some overlap in studies included in the systematic reviews.
- Patient selection criteria varied between studies.

Existing assessments of this procedure

International expert consensus guidance was published by the TaTME guidance group in 2020 (Adamina 2020). This includes guidance statements on indications, surgical quality and training and implementation of TaTME. The full text is included in the committee papers.

Consensus guidelines were published by the St. Gallen Colorectal Consensus Expert Group in 2018 (Adamina 2018). An expert radiologist, pathologist, and medical oncologist provided recommendations to maximise relevance to current practice. Consensus was obtained on all 7 different chapters: patient selection and surgical indication, perioperative management, patient positioning and operating room set up, surgical technique, devices and instruments, pelvic anatomy, TaTME training, and outcomes analysis.

Related NICE guidance

Below is a list of NICE guidance related to this procedure.

Interventional procedures

- Low-energy contact X-ray brachytherapy (the Papillon technique) for locally advanced rectal cancer. NICE interventional procedures guidance 659 (2019). Available from http://www.nice.org.uk/guidance/IPG659
- Low energy contact X-ray brachytherapy (the Papillon technique) for early stage rectal cancer. NICE interventional procedures guidance 532 (2015). Available from http://www.nice.org.uk/guidance/IPG532
- Preoperative high dose rate brachytherapy for rectal cancer. NICE interventional procedures guidance 531 (2015). Available from http://www.nice.org.uk/guidance/IPG531

NICE guidelines

- Colorectal cancer. NICE guideline 151 (2020). Available from http://www.nice.org.uk/guidance/NG151

Additional information considered by IPAC

Professional experts' opinions

Expert advice was sought from consultants who have been nominated or ratified by their professional Society or Royal College. The advice received is their individual opinion and is not intended to represent the view of the society. The advice provided by professional experts, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate. Two Professional expert questionnaires for TaTME for rectal cancer was submitted and can be found on the NICE website.

Patient commentators' opinions

NICE's Public Involvement Programme was unable to gather patient commentary for this procedure.

Company engagement

A structured information request was sent to 3 companies who manufacture a potentially relevant device for use in this procedure. NICE received 2 completed submissions. These was considered by the IP team and any relevant points have been taken into consideration when preparing this overview.

Issues for consideration by IPAC

- The Association of Coloproctology of Great Britain and Ireland (ACPGBI) has recommended a pause for re-evaluation and consolidation of evidence on the transanal TME approach to resecting rectal cancer, while awaiting the results of the COLOR III trial and pending further guidance (Fearnhead 2020).
- Ongoing trials
    - COLOR III: A Multicentre Randomised Clinical Trial Comparing Transanal TME Versus Laparoscopic TME for Mid and Low Rectal Cancer (NCT02736942); RCT; international (including UK); n=1,104; estimated study completion date May 2025
    - Transanal Versus Laparoscopic Total Mesorectal Excision For Mid And Low Rectal Cancer. A Multicentre Randomised Clinical Trial on Anastomotic Leak (NCT03413904); RCT; Italy; n=184; estimated study completion date February 2023
    - Prospective Randomized Clinical Trial for no Inferiority With Preoperative Chemoradiotherapy and Transanal Endoscopic Microsurgery (TEM) Versus Total Mesorectal Excision in T2-T3s N0, M0 Rectal Cancer (NCT01308190); RCT; Spain; n=173; estimated study completion date July 2021
    - Transanal Versus Laparoscopic Total Mesorectal Excision for Mid And Low Rectal Cancer in China (TLTME): A Single-center Randomized Clinical Trial (NCT03359616); RCT; China; n=258; estimated study completion date January 2022

- Transanal Versus Laparoscopic Total Mesorectal Excision For Mid And Low Rectal Cancer (TaLaR): A Multicentre Randomised Clinical Trial (NCT02966483); RCT; China; n=1,114; estimated study completion date July 2025

- Transanal Total Mesorectal Excision Versus Robotic Total Mesorectal Excision for Mid and Low Rectal Cancer: A Prospective Randomized Controlled Trial (NCT04091620); RCT; China; n=108; estimated study completion date October 2022

- Chinese Transanal Total Mesorectal Excision Registry Collaborative: A Nationwide Registry Study (NCT03416699); observational single-arm; China; n=300; estimated study completion date November 2021

- Rectal Surgery Evaluation Trial (RESET): Laparotomy vs Laparoscopy vs Robotic vs TaTME Rectal Surgery Matched Parallel Cohort Trial for High Surgical Risk Cancer Patients, With Mid- to Low Rectal Cancer (NCT03574493); Observational cohort; France; n=1,300; estimated study co0mpletion date December 2023

- Robotic vs. TaTME Rectal Surgery (ROTA STUDY) Matched Cohort Trial for Mid to Low Rectal Cancer Surgery Evaluation Trial in the Hands of an Experienced Surgeon (NCT04200027); Observational cohort; Denmark and UK; n=330; estimated study completion date November 2022

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5. Detering R, Roodbeen SX, van Oostendorp SE et al. (2019) Three-year nationwide experience with transanal total mesorectal excision for rectal cancer in the Netherlands: a propensity score-matched comparison with conventional laparoscopic total mesorectal excision. Journal of the American College of Surgeons 228: 235–44
6. de Lacy FB, Roodbeen SX, Rios J et al (2020) Three-year outcome after transanal versus laparoscopic total mesorectal excision in locally advanced rectal cancer: a multicenter comparative analysis. BMC Cancer 20: 677
7. Caycedo-Marulanda A, Lee L, Chadi SA et al. (2021) Association of transanal total mesorectal excision with local recurrence of rectal cancer. JAMA Network Open 4: e2036330
8. Yao H, An Y, Zhang H et al. (2021) Transanal total mesorectal excision: short-term outcomes of 1283 cases from a nationwide registry in China. Diseases of the Colon and Rectum 64: 190–99
9. Roodbeen SX, Spinelli A, Bemelman WA et al. (2020) Local recurrence after transanal total mesorectal excision for rectal cancer: a multicenter cohort study. Annals of Surgery doi: 10.1097/SLA.0000000000003757
10. Denost Q, Loughlin P, Chevalier R et al. (2018) Transanal versus abdominal low rectal dissection for rectal cancer: long-term results of the Bordeaux' randomized trial. Surgical Endoscopy 32: 1486–94
11. Zeng Z, Luo S, Chen J et al. (2019) Comparison of pathological outcomes after transanal versus laparoscopic total mesorectal excision: a prospective study using data from randomized control trial. Surgical Endoscopy 34: 3956–62

12. Ren J, Liu S, Luo H et al. (2021) Comparison of short-term efficacy of transanal total mesorectal excision and laparoscopic total mesorectal excision in low rectal cancer. Asian Journal of Surgery 44: 181–85

13. Dickson E, Penna M, Cunningham C et al. (2019) Carbon dioxide embolism associated with transanal total mesorectal excision surgery: a report from the international registries. Disease of the Colon and Rectum 62: 794–801

14. Perdawood SK (2018) A case of local recurrence following transanal total mesorectal excision: a new form of port-site metastasis? Techniques in Coloproctology 22: 319–20

15. Balaphas A, Dumont C, Faes S et al. (2018) Colonic conduit prolapse after transanal total mesorectal excision (taTME). Techniques in Coloproctology 22: 475–77

16. Alimova I, Chernyshov S, Nagudov M et al. (2021) Comparison of oncological and functional outcomes and quality of life after transanal or laparoscopic total mesorectal excision for rectal cancer: a systematic review and meta-analysis. Techniques in Coloproctology 25: 901–13

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19. Van Oostendorp SE, Kusters M, Bonjer HJ et al. (2021) The learning curve of transanal total mesorectal excision for rectal cancer is associated with local recurrence: results from a multicentre external audit. Colorectal Disease 23: 2020–29

20. Hompes R et al. (2020) International expert consensus guidance on indications, implementation and quality measures for transanal total mesorectal excision. Colorectal Disease 22: 749–55 https://doi.org/10.1111/codi.15147

21. Fearnhead NS, Acheson AG, Brown SR et al. (2020) The ACPGBI recommends pause for reflection on transanal total mesorectal excision. Colorectal Disease 22: 745–48

22. Adamina, Michel; Buchs, Nicolas C; Penna, Marta; et al. (2018) St. Gallen consensus on safe implementation of transanal total mesorectal excision. Surgical Endoscopy 32: 1091–103

Literature search strategy

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	13/08/2021	Issue 8 of 12, August 2021
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	13/08/2021	Issue 8 of 12, August 2021
International HTA database (INAHTA)	13/08/2021	-
MEDLINE (Ovid)	13/08/2021	1946 to August 12, 2021
MEDLINE In-Process (Ovid)	13/08/2021	1946 to August 12, 2021
MEDLINE Epubs ahead of print (Ovid)	13/08/2021	August 12, 2021
EMBASE (Ovid)	13/08/2021	1974 to 2021 August 12

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

Literature search strategy

Number	Search term
1	(TME or TAMIS or taTME).tw.
2	((transanal* or trans-anal*) adj4 minim* invas* surg*).tw.
3	natural orifice endoscopic surgery/ or transanal endoscopic surgery/
4	total* mesorect* excision*.tw.
5	((mesorect* or transanal* or trans-anal* or transrect* or trans-rect*) adj4 (excision* or dissect* or cut* or remove*)).tw.
6	or/1-5
7	*Rectal Neoplasms/
8	(rect* adj4 (cancer* or neoplasm* or lesion* or tumour* or tumor* or malignan* or carcinoma* or adenocarcinoma*)).tw.
9	7 or 8
10	6 and 9
11	animals/ not Humans/
12	10 not 11

13	limit 12 to english language

Appendix

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the summary of the key evidence. It is by no means an exhaustive list of potentially relevant studies.

Case series with fewer than 100 patients were excluded.

Additional papers identified

Article	Number of patients/ follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Abbott SC, Stevenson AR L, Bell SW et al. (2018) An assessment of an Australasian pathway for the introduction of transanal total mesorectal excision (taTME). Colorectal Disease 20: o1–o6	Case series n=133 (84% rectal cancer)	There was 1 technique-specific visceral injury, which occurred before the surgeon completed the training pathway. There were no cases of postoperative mortality; morbidity occurred in 27%. The DRM was clear in all cases of rectal cancer, and the CRM was positive in 2 cases. An intact or nearly intact TME was obtained in more than 98% of cases.	Studies with more patients or longer follow up are included.
Alhanafy MK, Park SS, Park SC et al. (2020) Early experience with transanal total mesorectal excision compared with laparoscopic total mesorectal excision for rectal cancer: a propensity score-matched analysis. Diseases of the Colon and Rectum 63: 1500–10	Non-randomised comparative study n=722 (202 matched pairs) follow up =median 34 months	Complete or nearly complete TME was 98% and 97% in the laparoscopic and transanal groups (p=0.41). Postoperative complications with Clavien-Dindo grade 3 or higher did not differ statistically significantly between groups (p=0.54) but were statistically significantly higher in patients with tumours less than 5 cm from the anal verge who had laparoscopy (laparoscopic group =12%; transanal group=2%; p=0.04). There were no statistical differences in the 3-year overall survival, recurrence-free survival, or local	Studies with more patients or longer follow up are included.

		recurrence rates between groups.	
Araujo SE, Perez RO, Seid VE et al. (2016) Laparo-endoscopic Transanal Total Mesorectal Excision (TATME): evidence of a novel technique. Minimally Invasive Therapy & Allied Technologies: MITAT 25: 278–87	Review n=721 (32 studies)	Little is known about long-term oncologic outcomes, intestinal, sexual, urinary function and quality of life after TATME. Multicentre large sample randomised controlled trials are needed for further investigation of these issues.	More recent systematic reviews are included.
Araujo SE, Crawshaw B, Mendes CR et al. (2015) Transanal total mesorectal excision: a systematic review of the experimental and clinical evidence. Techniques in coloproctology 19: 69–82	Systematic review n=150 (16 studies)	Involvement in CRMs was detected in 16 (12%) patients. For morbidity, pneumo-retroperitoneum, damage to the urethra, and air embolism were reported intraoperatively. Postoperative complications occurred in 34 (23%) patients. Oncologic safety parameters seem to be adequate although the evidence relies on small retrospective series done by highly trained surgeons.	More recent systematic reviews are included.
Arunachalam L, O'Grady H, Hunter IA et al. (2016) A systematic review of outcomes after transanal mesorectal resection for rectal cancer. Diseases of the Colon and Rectum 59: 340–50	Systematic review n=449 (15 studies) follow up =median 14.7 months	The operative mortality rate was 0.4% and the cumulative morbidity rate 36%. CRMs were clear in 98%, and the resected mesorectum was grade 3 in 87% of patients. There were 4 local recurrences (2%) and 12 patients (6%) with metastatic disease.	More recent systematic reviews are included.
Aubert M, Mege D, Panis Y (2019) Total mesorectal excision for low and middle rectal cancer: laparoscopic versus transanal approach-a meta-analysis. Surgical Endoscopy	Systematic review n=1,042 (14 studies)	This meta-analysis based on non-randomised studies suggests that TaTME seems better than laparoscopic TME in terms of overall and major morbidities, anastomotic leak, readmission rate, CRM involvement, and length of stay. These results need to be confirmed by randomised controlled trials.	More recent systematic reviews are included.

Bedrikovetski S, Dudi-Venkata NN, Kroon HM et al. (2020) Outcomes of minimally invasive versus open proctectomy for rectal cancer: a propensity-matched analysis of bi-national colorectal cancer audit data. Diseases of the Colon and Rectum 63: 778–87	Non-randomised comparative study n=3,451 (85 TaTME)	In this patient population, minimally invasive proctectomy demonstrated similar margin rates in comparison with open proctectomy, with a reduced length of stay but a higher overall complication rate.	Only a small proportion of patients had TaTME.
Bjoern MX, Perdawood SK (2020) Manometric assessment of anorectal function after transanal total mesorectal excision. Techniques in Coloproctology 24: 231–36	Non-randomised comparative study n=48 follow up =mean 41 months	Following TME surgery, the resting and squeeze pressures of the anal sphincter measured by manometry were generally decreased, with no differences between the transanal and laparoscopic approaches.	Studies with more patients or longer follow up are included.
Bjoern MX, Nielsen S, Perdawood SK (2019) Quality of life after surgery for rectal cancer: a comparison of functional outcomes after transanal and laparoscopic approaches. Journal of Gastrointestinal Surgery 23: 1623–30	Non-randomised comparative study n=85 follow up =mean 23 months (TaTME)	Anorectal dysfunction may occur after TME regardless of surgical technique, frequently more after TaTME. The LARS symptoms and the overall quality of life status were comparable. TaTME had a positive impact on the reported quality of life related to urinary symptoms.	Studies with more patients or longer follow up are included.
Bjorn MX, Perdawood SK (2015) Transanal total mesorectal excision--a systematic review. Danish Medical Journal 62	Systematic review n=336 (29 studies)	The preliminary results are encouraging, and the most serious complication is urethral injury. The oncological results are acceptable, although the follow up is short.	More recent systematic reviews are included.
Buchs NC, Nicholson GA, Ris F	Review	The preliminary data on complications and short-term	More recent systematic

et al. (2015) Transanal total mesorectal excision: A valid option for rectal cancer? World Journal of Gastroenterology 21: 11700–8		oncological outcomes are good, but also emphasise the importance of careful patient selection. There is a need for large-scale trials focusing on long-term outcomes and oncological safety.	reviews are included.
Caycedo-Marulanda A, Nadeau K, Verschoor CP et al. (2021) Exploring the perioperative outcomes of a sample of successful adopters of transanal total mesorectal excision (taTME) during the learning phase. Surgery 169: 774–81	Case series n=366 follow up =median 35 months	Local recurrence rate=4% Among implementation and postimplementation groups local recurrence was 7.5% and 3.1%, respectively, and the rate of local recurrence was nearly 60% lower in the postimplementation group (HR=0.43, 95% CI 0.26 to 0.72). TME specimens were complete or nearly complete in 88% of cases, and the circumferential and distal margins were clear in 93.2% and 92.6%, respectively.	Studies with more patients or longer follow up are included.
Caycedo-Marulanda A, Verschoor CP (2020) Experience beyond the learning curve of transanal total mesorectal excision (taTME) and its effect on the incidence of anastomotic leak. Techniques in Coloproctology 24: 309–16	Case series n=100	6 cases of anastomotic leak occurred over the course of the study, the last of which was in the 37th patient. Relative to a baseline anastomotic leak rate of 8%, cumulative sum analysis indicated that a 50% improvement in risk occurred at trial 50 of 85 patients that had an anastomosis done. Two patients developed local recurrence during the study period. No correlation between learning curve and oncologic outcomes was identified.	Studies with more patients or longer follow up are included.
Chang TC, Kiu KT (2018) Transanal total mesorectal excision in lower rectal cancer: Comparison of short-term outcomes with conventional laparoscopic total mesorectal excision.	Non-randomised comparative study n=92	The estimated blood loss, duration of operation, and postoperative complications were similar between both groups. For pathological outcomes, no patients with CRM less than 1 mm were seen in the TaTME group compared with 4 patients in	Studies with more patients or longer follow up are included.

Journal of Laparoendoscopic & Advanced Surgical Techniques. 28: 365–9		the laparoscopic group (p=0.037).	
Chen CC, Lai YL, Jiang JK et al. (2016) Transanal total mesorectal excision versus laparoscopic surgery for rectal cancer receiving neoadjuvant chemoradiation: a matched case-control study. Annals of Surgical Oncology 23: 1169–76	Non-randomised comparative study n=150	The TaTME group yielded longer distal margin lengths. No statistically significant differences were seen in blood loss, intraoperative complication rate, conversion rate, anastomosis type, and free circumferential margin rate.	Studies with more patients or longer follow up are included.
Chen YT, Kiu KT, Yen MH et al. (2019) Comparison of the short-term outcomes in lower rectal cancer using three different surgical techniques: Transanal total mesorectal excision (TME), laparoscopic TME, and open TME. Asian Journal of Surgery 42: 674–80	Non-randomised comparative study n=126 follow up =median 26 months	In the short-term outcomes, TaTME achieved better pathological results and disease-free survival than open TME but not statistically significantly superior to laparoscopic TME. Further studies are necessary to evaluate the long-term oncological results.	Studies with more patients or longer follow up are included.
Chevallay M, Meyer J, Wassmer C-H et al. (2019) Current trends in the management of low rectal tumors: transanal total mesorectal excision. Current Colorectal Cancer Reports 2019	Review	When compared with laparoscopic or robotic TME, the taTME showed to be safe with similar oncological results. Patients known to be difficult, male, obese, with a narrow pelvis, should be considered for the taTME approach.	More recent systematic reviews are included.
Cooper M, Kim J, Shin BNH et al. (2020) Transanal	Non-randomised	Mesorectal completeness was obtained in 47% in the taTME group compared with 78% in	Studies with more patients or longer

total mesorectal excision the Gold Coast experience: learning curve and comparison to traditional technique. ANZ Journal of Surgery 90: 1316–20	comparative study n=43	the anterior resection group (p=0.115). 6% of patients in the taTME group had positive CRM compared with none in the anterior resection group. Conversion rates were greater in the taTME group (15% versus 0%, p=0.028). Operative time, length of stay and Clavien 4 and 5 complications were greater in the taTME group.	follow up are included.
de'Angelis N, Portigliotti L, Azoulay D et al. (2015) Transanal total mesorectal excision for rectal cancer: a single center experience and systematic review of the literature. Langenbeck's Archives of Surgery 400: 945–59	Non-randomised comparative study n=64	One patient in the TaTME group and 2 patients in the laparoscopic TME group developed local recurrence. The estimated survival rate at 2 years was 95.5% and 96.6% respectively (p=0.646).	Studies with more patients or longer follow up are included.
Deijen CL, Tsai A, Koedam et al. (2016) Clinical outcomes and case volume effect of transanal total mesorectal excision for rectal cancer: a systematic review. Techniques in Coloproctology 20: 811–24	Systematic review n=794 (33 studies)	Conversion rate=3% Complication rate=40% (11.5% were major complications) The quality of the mesorectum was complete in 88%, and the CRM was involved in 5%. In low- versus high-volume centres, the conversion rate was 4% versus 3%, and major complication rates were 12% versus 10.5%, respectively. TME quality was complete in 80.5% versus 90%, and CRM involvement was 4.8% and 4.5% in low- versus high-volume centres, respectively.	More recent systematic reviews are included.
de Lacy FB, van Laarhoven JJ, Pena R et al. (2018) Transanal total mesorectal excision: pathological results	Case series n=186	The composite of complete mesorectal excision, negative CRM, and negative DRM was achieved in 88% of patients.	Studies with more patients or longer follow up are included.

of 186 patients with mid and low rectal cancer. Surgical Endoscopy 32: 2442–47			
Dittrich L, Biebl M, Schmuck R et al. (2021) Initial experience with the safe implementation of transanal total mesorectal excision (Tatme) as a standardized procedure for low rectal cancer. Journal of Clinical Medicine 10: 1–15	Case series n=157 follow up =mean 19.5 months	Early anastomotic leakage occurred in 7% of patients. Mesorectum specimen was complete in 87%, R1 resection rate was 4.5% (involved DRM) and in 8%, the CRM was positive. The 3-year local recurrence rate of 58 patients with a follow up of 36 or more months was 3%. Overall survival was 92% after 12 months, and 82% after 36 months.	Studies with more patients or longer follow up are included.
2017 European Society of Coloproctology (ESCP) collaborating group (2018) An international multicentre prospective audit of elective rectal cancer surgery; operative approach versus outcome, including transanal total mesorectal excision (TaTME). Colorectal Disease 20 suppl 6: 33–46	Non-randomised comparative study n=2,579 (20% were transanal)	On univariate analysis both laparoscopic TaTME (OR 1.61, 1.02 to 2.48, p=0.04) and robotic TaTME (OR 3.05, 1.10 to 7.34, p=0.02) were associated with a higher risk of anastomotic leak than non-transanal laparoscopic TME. However, this association was lost in the mixed-effects model controlling for patient and disease factors (OR 1.23, 0.77 to 1.97, p=0.39 and OR 2.11, 0.79 to 5.62, p=0.14 respectively), whilst low rectal anastomosis (OR 2.72, 1.55 to 4.77, p<0.001) and male gender (OR 2.29, 1.52 to 3.44, p<0.001) remained strongly associated. The overall positive circumferential margin resection rate was 4%, which varied between operative approaches: laparoscopic 3%, transanal 4%, open 5%, robotic 1%.	The study focused on risk factors for anastomotic leak.
Fernandez-Hevia M, Delgado S, Castells A et al. (2014) Transanal total mesorectal excision	Non-randomised comparative study	Evaluation of short-term outcomes demonstrated that transanal TME is a feasible and safe technique associated with a shorter surgical time	Studies with more patients or longer

in rectal cancer: short-term outcomes in comparison with laparoscopic surgery. Ann. Surg. doi: 10.1097/ SLA.0000000000000865	n=74 follow up =30 days	and a lower early readmission rate.	follow up are included.
Filips A, Haltmeier T, Kohler A et al. (2021) LARS is associated with lower anastomoses, but not with the transanal approach in patients undergoing rectal cancer resection. World Journal of Surgery 45: 873–79	Non-randomised comparative study n=80 follow up =6 months	50% of patients in this cohort had some LARS symptoms after a mid- or low-rectal cancer resection. LARS scores were negatively correlated with the distance of the anastomosis from the anal verge. After adjustment for the height of the anastomosis, TaTME was not associated with higher LARS at 6 months when compared with low anterior resection with a TME.	Studies with more patients or longer follow up are included.
Foo CC, Kin Ng K, Tsang JS et al. (2020) Low anterior resection syndrome after transanal total mesorectal excision: a comparison with the conventional top-to-bottom approach. Diseases of the Colon and Rectum 63: 497–503	Non-randomised comparative study n=70 follow up =12 months	At 3 months, the median LARS score was 37 after TaTME, which was statistically significantly higher than the conventional approach, 32 (p=0.045). Apart from this, the LARS score, severity grading, and the Wexner score were comparable at 6 and 12 months.	Studies with more patients or longer follow up are included.
Gachabayov M, Tulina I, Bergamaschi R et al. (2019) Does transanal total mesorectal excision of rectal cancer improve histopathology metrics and/or complication rates? A meta-analysis. Surgical Oncology 30: 47–51	Systematic review n=1,572 (6 studies)	This meta-analysis found that taTME of rectal cancer does not improve histopathology metrics and complication rates when compared with robotic TME.	More recent systematic reviews are included.

Gerken M, Klinkhammer-Schalke M, Schatz S et al. (2021) Transanal total mesorectal excision: short- and long-term results of the first hundred cases of a certified colorectal cancer center in Germany. Surgical Endoscopy 2021	Case series n=100 follow up =median 2.7 years	3-year cumulative incidence rate for local recurrence was 2.2% and a 3-year local recurrence-free survival of 81.9%. 3-year overall survival was 82.9%, and 3-year disease-free survival was 75.7%.	Studies with more patients or longer follow up are included.
Gonzalez-Abos C, de Lacy FB, Guzman Y et al (2021) Transanal total mesorectal excision for stage II or III rectal cancer: pattern of local recurrence in a tertiary referral center. Surgical Endoscopy https://doi.org/10.1007/s00464-020-08200-4	Case series n=205 follow up =median 34 months	Mesorectal specimen quality was complete or near complete in 98.5%, while CRM was 1 mm or less in 12%. 7 (3%) patients had local recurrent disease, 6 of whom also had haematogenous metastases.	Studies with more patients or longer follow up are included.
Gordeyev SS, Dzhumabaev KE, Mamedli ZZ et al. (2019) Transanal total mesorectal excision in selected patients with "difficult pelvis": a case-control study of "difficult" rectal cancer patients. European Surgery - Acta Chirurgica Austriaca 51: 13–18	Non-randomised comparative study n=52 follow up =median 28 months	Stapling anastomosis was done in 17 (68%) patients in the laparoscopic group and 21 (84%) patients in the TaTME group (p=0.2). There was 1 distant failure in each group and 1 patient in the laparoscopic group developed a local recurrence.	Studies with more patients or longer follow up are included.
Grass JK, Perez DR, Izbicki JR et al. (2019) Systematic review analysis of robotic and transanal approaches in TME	Systematic review n=10,288 (570 taTME, 4084	The level of evidence is still low. Oncological outcome seems to be comparable following taTME and robotic TME. Results of disease-specific survival and local recurrence are currently not	No meta-analysis. More recent systematic reviews are included.

surgery - A systematic review of the current literature in regard to challenges in rectal cancer surgery. European Journal of Surgical Oncology 45: 498–509	laparoscopic TME and 5758 robotic TME) 64 studies	available for these latest techniques. But positivity of circumferential margin is described to be at least equivalent for robotic TME to laparoscopic TME and has been found to be superior in taTME in comparison with laparoscopic TME.	
Hasegawa S, Takahashi R, Hida K et al. (2016) Transanal total mesorectal excision for rectal cancer. Surgery Today 46: 641–53	Review	The approach seems to be feasible for the operative and short-term postoperative outcomes. In experienced hands, transanal TME is a promising method for the resection of mid- and low-rectal cancers. Further investigations are needed to clarify the long-term oncological and functional outcomes.	More recent systematic reviews are included.
Ho M-F, Ng DC-K, Lee JF-Y et al. (2021) Should transanal total mesorectal excision be implemented in medium-sized colorectal unit? Technical and oncological outcome. Annals of Coloproctology; 2021	Non-randomised comparative study n=80 follow up =median 39 months	It is technically feasible and oncologically safe to do TaTME in a medium-volume colorectal unit. Patients with difficult pelvic anatomy can benefit by reducing the risk of conversion and margin positivity rate.	Studies with more patients or longer follow up are included.
Hol JC, Burghgraef TA, Rutgers MLW et al. (2021) Comparison of laparoscopic versus robot-assisted versus transanal total mesorectal excision surgery for rectal cancer: a retrospective propensity score-matched cohort	Non-randomised comparative study (propensity score matched) n=1,078 (244 TaTME, 490 laparoscopic, 344	Conversion rates were 3.7, 4.6 and 1.9 per cent in laparoscopic, robot assisted and TaTME respectively (P = 0.134). The number of incomplete specimens, circumferential resection margin involvement rate and morbidity rates did not differ.	A study from the same data source is already included (Detering, 2019).

study of short-term outcomes. The British Journal of Surgery 2021	robot-assisted); 108 in each group after matching.		
Hol JC, van Heek NT, de Jong GM et al. (2021) Morbidity and costs of diverting ileostomy in transanal total mesorectal excision with primary anastomosis for rectal cancer. Techniques in Coloproctology; 2021	Case series n=147 follow up =1 year	Morbidity and associated costs after diverting ileostomy are high. The incidence and morbidity of anastomotic leakage was not reduced by creation of an ileostomy. Omission of a diverting ileostomy after TaTME could possibly result in a reduction in treatment associated morbidity and costs.	Study focuses on the use of a diverting ileostomy
Hol JC, van Oostendorp SE, Tuynman JB et al. (2019) Long-term oncological results after transanal total mesorectal excision for rectal carcinoma. Techniques in Coloproctology 23: 903–11	Case series n=159 follow up =mean 55 months	The 3-year local recurrence rate was 2% and the 5-year local recurrence rate was 4%. Median time to local recurrence was 19 months. Distant metastases were found in 22 (14%) patients and were diagnosed after a median of 6.9 months (range 1.1 to 50.4) months. Disease-free survival was 92% at 3 years and 81% at 5 years. Overall survival was 83.6% at 3 years and 77.3% at 5 years.	Studies with more patients or longer follow up are included.
Hu Dongping, Jin Penghui, Hu Lidong et al. (2018) The application of transanal total mesorectal excision for patients with middle and low rectal cancer: A systematic review and meta-analysis. Medicine 97: e11410	Systematic review n=859 (13 studies)	For complete tumour resection and positive circumferential margins in the TaTME group, the ORs and 95% CIs were 1.93 and 1.09 to 3.42 (p=0.02) and 0.43 and 0.22 to 0.82 (p=0.01), respectively. Rates of postoperative complications were similar in the 2 groups, and differences in the risk of ileus and anastomotic leakage were not statistically significant.	More recent systematic reviews are included.
Huscher CGS, Lirici MM (2017) Transanal total	Case series n=102	Postoperative morbidity was 33%. Mortality rate at 30 days was 2% (n=2). Quality of	Studies with more patients or longer

mesorectal excision: pneumodissection of retroperitoneal structures eases laparoscopic rectal resection. Diseases of the Colon and Rectum 60: 1109–12		mesorectal excision was complete in 99 cases (97%) and nearly complete in 3% of cases.	follow up are included.
Jiang T-Y, Ma J-J, Zheng M-H (2021) Controversies and consensus in transanal total mesorectal excision (taTME): Is it a valid choice for rectal cancer? Journal of Surgical Oncology 123 (supp 1) 59-64	Review	TaTME is a feasible option for colorectal surgery in the treatment of rectal cancer, particularly in patients with low rectal cancer. The improvement of taTME and its application depends on the following points: 1. Standardised guidelines 2. A formatted training program. The minimum number of training procedures necessary in taTME surgery should be quantified. 3. More studies on the long-term oncologic outcomes and quality of life. 4. More high-quality, well-designed RCTs.	Review without a meta-analysis.
Jiang HP, Li YS, Wang B et al. (2018) Pathological outcomes of transanal versus laparoscopic total mesorectal excision for rectal cancer: a systematic review with meta-analysis. Surgical Endoscopy 32: 2632–42	Systematic review n=762 (10 studies)	TaTME had more advantages on positive CRM, CRM, and DRM compared with laparoscopic TME. No benefits of taTME on pathological outcomes were detected. Randomised controlled trials with adequate power are needed.	More recent systematic reviews are included.
Jouppe P-O, Courtot L, Sindayigaya R et al. (2020) Trans-anal total mesorectal excision in low rectal cancers: Preliminary oncological results of a comparative	Non-randomised comparative study n=41 follow up =median 20	More patients had a positive CRM in the abdominoperineal resection group (48% versus 5%, p<0.0036). The difference in complication rates between the 2 groups was not statistically significant. The local recurrence rate did not	Studies with more patients or longer follow up are included.

study. Journal of Visceral Surgery	months (TaTME)	differ between the 2 groups (5% in both).	
Kang L, Chen Y-G, Zhang H et al. (2020) Transanal total mesorectal excision for rectal cancer: A multicentric cohort study. Gastroenterology Report 8: 36–41	Case series n=211 follow up =median 35 months	Overall rate of complications was 28%. 83% (175/211) of patients had complete TME and 16% had near complete TME. The CRM was negative in 98% of patients. Mortality=8%, local recurrence=6%, systemic recurrence=13% Kaplan-Meier survival analysis showed that 1-, 2-, and 3-year disease-free survival rates were 95%, 89%, and 80%, respectively, and 1-, 2-, and 3-year overall survival rates were 97%, 96% and 93%, respectively.	Studies with more patients or longer follow up are included.
Klein MF, Seiersen M, Bulut O et al. (2020) Short-term outcomes after transanal total mesorectal excision for rectal cancer in Denmark - a prospective multicentre study. Colorectal Disease https://doi.org/ 10.1111/codi.15454	Case series n=115 follow up =median 23 months	Anastomotic leakage occurred in 6/109 (6%). One urethral injury occurred. Non-microradicality was seen in 8% (R1, 6%; R2, 2%). Four local recurrences occurred, 1 of which was multifocal.	Studies with more patients or longer follow up are included.
Koedam TWA, Veltcamp HM, Penna M et al. (2019) Short-term outcomes of transanal completion total mesorectal excision (cTaTME) for rectal cancer: a case-matched analysis. Surgical Endoscopy 33: 103–9	Non-randomised comparative study n=50	TaTME after full-thickness excision is a promising technique with a statistically significantly lower risk of perforation of the rectum and better specimen quality compared with conventional completion TME.	Studies with more patients or longer follow up are included.
Koedam TWA, Veltcamp Helbach M, van de Ven PM	Case series n=138	The learning curve of TaTME affected major (surgical) postoperative complications for	Studies with more patients or longer

et al. (2018) Transanal total mesorectal excision for rectal cancer: evaluation of the learning curve. Techniques in Coloproctology 22: 279–87		the first 40 patients. A 2-team approach decreased operative time and conversion rate.	follow up are included.
Lacy AM, Tasende MM, Delgado S et al. (2015) Transanal total mesorectal excision for rectal cancer: outcomes after 140 patients. Journal of the American College of Surgeons 221: 415–23	Case series n=140 follow up =mean 15 months	There were no conversions or intraoperative complications. Macroscopic quality assessment of the resected specimen was complete in 97% and nearly complete in 2%. Thirty-day morbidity was minor in 24% and major in 10%. No patient died within the first 30 days after surgery. Local recurrence rate was 2% and systemic recurrence was 8%.	Studies with more patients or longer follow up are included.
Lau S, Kong J, Bell S et al. (2021) Transanal mesorectal excision: early outcomes in Australia and New Zealand. The British Journal of Surgery 108: 214–19	Case series n=308 follow up =median 22 months	The anastomotic leak rate was 8% and there was no mortality within 30 days of surgery. Pathological examination found a complete mesorectum in 295 patients (96%), a near-complete mesorectum in 7 patients (2%), and an incomplete mesorectum in 6 patients (2%). The circumferential resection margin and distal resection margin was involved in 9 patients (3%), and 2 patients (0.6%) respectively. The local recurrence rate was 2% and median time to local recurrence was 30.5 months.	Studies with more patients or longer follow up are included.
Law WL, Foo DCC (2019) Comparison of early experience of robotic and transanal total mesorectal excision using propensity score matching.	Non-randomised comparative study n=80	Both taTME and robotic surgery can achieve favourable outcomes in rectal cancer resection. Comparison of the early experience of the 2 procedures with propensity score matching showed the taTME was associated with a shorter operating time, less	Studies with more patients or longer follow up are included.

Surgical Endoscopy 33: 757–63		blood loss, and a higher rate of transanal extraction of the specimen. Further evaluation by randomised trials is warranted.	
Lee KY, Shin JK, Park YA et al. (2018) Transanal endoscopic and transabdominal robotic total mesorectal excision for mid-To-low rectal cancer: Comparison of short-Term postoperative and oncologic outcomes by using a case-matched analysis. Annals of Coloproctology 34: 29–35	Non-randomised comparative study n=45	Transanal endoscopic and transabdominal robotic TME showed similar histopathologic and postoperative outcomes except for estimated blood loss and the proximal resection margin for a select group of patients.	Studies with more patients or longer follow up are included.
Lee L, de Lacy B, Gomez Ruiz M et al. (2019) A multicenter matched comparison of transanal and robotic total mesorectal excision for mid and low-rectal adenocarcinoma. Annals of surgery 270: 1110–16	Non-randomised comparative study n=596	The incidence of poor-quality resection was 7% in both groups. There were no differences in TME specimen quality and CRM. DRM involvement may be higher after TaTME (1.8% compared with 0.3%, p=0.051).	Studies with more patients or longer follow up are included.
Lei P, Ruan Y, Yang X et al. (2018) Trans-anal or trans-abdominal total mesorectal excision? A systematic review and meta-analysis of recent comparative studies on perioperative outcomes and pathological result. International Journal	Systematic review n=1,346 (17 studies)	TaTME achieves similar surgical outcomes to laparoscopic TME, with the added advantage of a safe CRMs, reduced blood loss, shorter hospital stay, lower conversion and readmission rates, and lower postoperative morbidity. Long-term oncological and functional data are needed.	More recent systematic reviews are included.

of Surgery 60: 113–19			
Li Y, Bai X, Niu B et al. (2021) A prospective study of health related quality of life, bowel and sexual function after TaTME and conventional laparoscopic TME for mid and low rectal cancer. Techniques in Coloproctology 25: 449–59	Non-randomised comparative study n=60 follow up =12 months	Compared with patients with mid and low rectal cancer who had conventional laparoscopic TME, those who had TaTME had worse HRQoL and bowel function for a short period after primary resection but seem to have better sexual function in the long term.	Studies with more patients or longer follow up are included.
Lin D, Yu Z, Chen W et al. (2019) Transanal versus laparoscopic total mesorectal excision for mid and low rectal cancer: A meta-analysis of short-term outcomes. Videosurgery and Other Miniinvasive Techniques 14: 353–65	Systematic review n=899 (12 studies)	TaTME offers a safe and feasible alternative to laparoscopic TME although the clinicopathological features were not superior.	More recent systematic reviews are included.
Ma B, Gao P, Song Y et al. (2016) Transanal total mesorectal excision (taTME) for rectal cancer: a systematic review and meta-analysis of oncological and perioperative outcomes compared with laparoscopic total mesorectal excision. BMC Cancer 16: 380	Systematic review n=573 (7 studies)	In comparison with laparoscopic TME, taTME seems to achieve comparable technical success with acceptable oncologic and perioperative outcomes. However, multicentre randomised controlled trials are needed to further evaluate the efficacy and safety of taTME.	More recent systematic reviews are included.
Marks JH, Myers EA, Zeger EL et al. (2017) Long-term	Case series n=373	96% of TME specimens were complete or near complete, 94% had a negative CRM, and	Different techniques were used

outcomes by a transanal approach to total mesorectal excision for rectal cancer. Surgical Endoscopy 31: 5248–57	follow up =mean 5.5 years	98.6% had a negative distal margin. Perioperative morbidity and mortality rates were 13.4 and 0.3%. Overall local recurrence, distant metastasis and Kaplan–Meier 5-year actuarial survival were 7.4, 19.5, and 90%, respectively.	during the study period (1984 to 2015), including transanal abdominal transanal proctosigmoid-ectomy with coloanal anastomosis.
Marks J H, Montenegro G A, Salem J F et al. (2016) Transanal TATA/TME: a case-matched study of taTME versus laparoscopic TME surgery for rectal cancer. Techniques in coloproctology 20: 467–73	Non-randomised comparative study n=34	There were no differences in perioperative or postoperative outcomes or pathologic TME outcomes of transanal or bottom-up TME compared with standard laparoscopic TME.	Studies with more patients or longer follow up are included.
Matsuda T, Yamashita K, Hasegawa H et al. (2021) Clinical outcomes of transanal total mesorectal excision using a lateral-first approach for low rectal cancer: a propensity score matching analysis. Surgical Endoscopy 35: 971–78	Non-randomised comparative study n=56	TaTME using a lateral-first approach is feasible and may offer several advantages over laparoscopic TME in terms of short-term outcomes. It might be an alternative safe approach for taTME.	Studies with more patients or longer follow up are included.
Mege D, Hain E, Lakkis Z et al. (2018) Is trans-anal total mesorectal excision really safe and better than laparoscopic total mesorectal excision with a perineal approach first in patients with low	Non-randomised comparative study n=68 follow up =13 months (for TaTME)	The TaTME learning curve seems to be associated with a significant rate of intra-operative complications. Because no statistically significant benefit has been reported to date, more evidence is needed before TaTME can be considered as a better approach than laparoscopic TME with a	Studies with more patients or longer follow up are included.

rectal cancer? A learning curve with case-matched study in 68 patients. Colorectal Disease 20: o143-o151		perineal approach first in patients with low rectal cancer.	
Moon JY, Lee MR, Ha GW et al. (2021) Long-term oncologic outcomes of transanal TME compared with transabdominal TME for rectal cancer: a systematic review and meta-analysis. Surgical Endoscopy 2021	Systematic review n=2,143 (11 studies)	There were no statistically significant differences between the 2 groups in overall survival, disease-free survival, and local and distant recurrence with a RR of 0.65 (95% CI 0.39 to 1.09, I^2=0%), 0.79 (95% CI 0.57 to 1.10, I^2=0%), 1.14 (95% CI 0.44 to 2.91, I^2=66%), and 0.75 (95% CI 0.40 to 1.41, I^2=0%), respectively.	Other systematic reviews with more outcomes have been included.
Nguyen TX, Ho HT, Phan HT et al. (2021) The effectiveness of double team for transanal total mesorectal excision in treatment of mid-low rectal cancer. International Journal of Surgery Open 34: 100359	Non-randomised comparative study (single versus double team) n=72	The double-team TaTME in treatment of mid-low rectal cancer is effective with the shortness of operative time, the lower rate of the postoperative pre-sacral abscess, and LARS scores, while this method guaranteed the quality of mesorectal specimens and the disease-free survival rate.	Small study, comparing results with a single team against results with a double team.
Ong GK, Tsai B, Patron RL et al. (2020) Transanal total mesorectal excision achieves equivalent oncologic resection compared to laparoscopic approach, but with functional consequences. American Journal of Surgery 221: 566–69	Non-randomised comparative study n=50	TaTME may be a good option for the most distal tumours, when distal margins may be compromised. TaTME provides equivalent oncologic resection, but there is a higher incidence of postoperative faecal incontinence.	Studies with more patients or longer follow up are included.
Otero-Pineiro AM, Bravo R, Lacy AM (2021) TaTME: Present and future	Review	While satisfactory short-term results have been reported, it is a new technique, and long-term results and definitive	Review without a meta-analysis.

perspectives? Digestive Disease Interventions 2021		results from controlled trials are pending. As evidence of safety and feasibility accumulates, training programs structured to standardise teaching, training, and safe expansion will aid the safe spread of TaTME.	
Otero-Pineiro AM, de Lacy FB, Van Laarhoven JJ et al. (2021) The impact of fluorescence angiography on anastomotic leak rate following transanal total mesorectal excision for rectal cancer: a comparative study. Surgical Endoscopy 35: 754–62	Non-randomised comparative study n=284	Indocyanine green fluorescence angiography modified the proximal colonic transection in more than one-quarter of patients, leading to a statistically significant decrease in anastomotic leak rate.	Study focuses on the use of fluorescence angiography.
Penna M, Hompes R, Arnold S et al. (2019) Incidence and risk factors for anastomotic failure in 1594 patients treated by transanal total mesorectal excision results from the international TaTME registry. Annals of Surgery 269: 700–11	Registry n=1,594 (97% cancer)	The overall anastomotic failure rate was 16%. This included early (8%) and delayed leak (2%), pelvic abscess (5%), anastomotic fistula (1%), chronic sinus (1%), and anastomotic stricture in 4% of cases. Independent risk factors of anastomotic failure were: male sex, obesity, smoking, diabetes mellitus, tumours more than 25 mm, excessive intraoperative blood loss, manual anastomosis, and prolonged perineal operative time.	Study focuses on risk factors for anastomotic failure.
Penna M, Hompes R, Arnold S et al. (2017) Transanal total mesorectal excision: international registry results of the first 720 cases. Annals of Surgery 266: 111–17	registry n=720	Abdominal or perineal conversion was 6% and 3%, respectively. Intact TME specimens were achieved in 85%, with minor defects in 11% and major defects in 4%. R1 resection rate was 3%. Postoperative mortality and morbidity were 0.5% and 33% respectively.	Studies with more patients or longer follow up are included.

Penna M, Buchs NC, Bloemendaal AL et al. (2016) Transanal total mesorectal excision for rectal cancer: the journey towards a new technique and its current status. Expert Review of Anticancer Therapy 16: 1145–53	Review	The learning curve for this procedure remains to be established and a structured training programme is necessary to ensure safe introduction and dissemination of the technique in the clinical setting. Further innovation including stereotactic navigation and more specialised transanal equipment are currently being explored and are likely to enhance the technique further.	More recent systematic reviews are included.
Perdawood SK, Kroeigaard J, Eriksen M et al. (2021) Transanal total mesorectal excision: the Slagelse experience 2013-2019. Surgical Endoscopy 35: 826–36	Case series n=200 follow up =mean 29 months	Anastomotic leakage occurred in 9% of patients, and the overall rate of postoperative complications was 24.5%. The TME specimen was incomplete in 11% of patients, and the CRM was positive in 5.5% of patients. Local recurrence occurred in 7 patients with a follow up of at least 2 years (5%). Distant metastasis occurred in 12% of patients. The overall survival was 90% and disease-free survival was 81%.	Studies with more patients or longer follow up are included.
Perdawood SK, Thinggaard BS, Bjoern MX (2018) Effect of transanal total mesorectal excision for rectal cancer: comparison of short-term outcomes with laparoscopic and open surgeries. Surgical Endoscopy 32: 2312–21	Non-randomised comparative study n=300	TaTME resulted in lower rates of incomplete TME specimens than laparoscopic TME, but not open TME (p=0.016, p=0.750, respectively). The rates of CRM involvement, mean CRM distance, and the percentages of successful surgery were comparable among the 3 groups (p=0.368). TaTME resulted in shorter operation time and less blood loss than the other 2 groups (p<0.001 and p<0.001). Hospital stay was shorter in the TaTME group (p=0.002); complication rate and mortality were comparable among the groups.	Studies with more patients or longer follow up are included.

Perdawood SK, Al Khefagie GAA (2016) Transanal vs laparoscopic total mesorectal excision for rectal cancer: initial experience from Denmark. Colorectal Disease: the official journal of the Association of Coloproctology of Great Britain and Ireland 18: 51–8	Non-randomised comparative study n=50	The TaTME procedure had comparable pathological results and acceptable short-term postoperative outcomes compared with laparoscopic TME.	Studies with more patients or longer follow up are included.
Perez D, Melling N, Biebl M et al. (2018) Robotic low anterior resection versus transanal total mesorectal excision in rectal cancer: A comparison of 115 cases. European Journal of Surgical Oncology 44: 237–42	Non-randomised comparative study n=115	Both procedures should be considered equally feasible for low rectal cancer cases and as an alternative to conventional anterior resections (open or laparoscopic). Furthermore, both techniques allow excellent oncological outcome especially in patients with anatomical limitations.	Studies with more patients or longer follow up are included.
Persiani R, Agnes A, Belia F et al. (2020) The learning curve of TaTME for mid-low rectal cancer: a comprehensive analysis from a five-year institutional experience. Surgical Endoscopy https://doi.org/10.1007/s00464-020-08115-0	Case series n=121	TaTME had a learning curve of 71 cases for the mean operative time, 55 to 69 cases for major complications and reoperation, and 27 cases for anastomotic leakage.	Study focuses on learning curve.
Persiani R, Biondi A, Pennestri F et al. (2018) Transanal total mesorectal excision vs laparoscopic total mesorectal excision in the treatment of low and middle rectal cancer: a	Non-randomised comparative study n=92	Laparoscopic TME was associated with a higher conversion rate to open surgery (20% vs 0%, p=0.002). TaTME showed a longer DRM (15 mm versus 25 mm; p<0.001), and similar results for the completeness of mesorectal excision and CRM involvement, compared with	Studies with more patients or longer follow up are included.

propensity score matching analysis. Diseases of the Colon and Rectum 61: 809–16		laparoscopy. There were no statistically significant differences between the 2 groups in terms of postoperative complications.	
Pontallier A, Denost Q, Van Geluwe B et al. (2016) Potential sexual function improvement by using transanal mesorectal approach for laparoscopic low rectal cancer excision. Surgical Endoscopy 30: 4924–33	RCT n=72 follow up =median 38 months	Transanal approach for low rectal cancer did not change bowel and urologic functions compared with the conventional laparoscopic approach. However, there was a trend to a better erectile function with a statistically significantly higher rate of sexual activity in the transanal group.	The study presents functional outcomes for a relatively small number of patients who were included in the RCT that has already been described (Denost 2018).
Rasulov AO, Mamedli ZZ, Gordeyev SS et al. (2016) Short-term outcomes after transanal and laparoscopic total mesorectal excision for rectal cancer. Techniques in Coloproctology 20: 227–34	Non-randomised comparative study n=45	There was no post-operative mortality and post-operative morbidity in the taTME and laparoscopic TME groups was similar (27 versus 26%). One patient in the taTME group had positive CRMs. Oncologic results from resected specimens were comparable.	Studies with more patients or longer follow up are included.
Rausa E, Bianco F, Kelly ME et al. (2019) Systemic review and network meta-analysis comparing minimal surgical techniques for rectal cancer: quality of total mesorectum excision, pathological, surgical, and oncological outcomes. Journal of Surgical Oncology 119: 987–98	Systematic review	All 3 surgical techniques are comparable across TME quality and oncological outcomes. Ultimately, good outcomes are based on each individual surgeon choosing an approach based on their expertise.	More recent systematic reviews are included.

Ren J, Luo H, Liu S et al. (2021) Short- and mid-term outcomes of transanal versus laparoscopic total mesorectal excision for low rectal cancer: a meta-analysis. Annals of Surgical Treatment and Research 100: 86–99	Systematic review n=772 (10 studies)	Compared with the laparoscopic group, the conversion rate was low (risk ratio [RR] 0.25; 95% CI 0.11 to 0.54, p<0.001), the CRM involvement was low (RR 0.48; 95% CI, 0.27 to 0.86, p=0.010), and the hospital stay was short (MD –1.72, 95% CI -2.89 to -0.55, p=0.004) in the TaTME group. No statistically significant differences were seen in the mesorectal resection quality, CRM distance, DRM involvement, DRM distance, local R1 resection, intraoperative complications, morbidity, anastomotic leakage, severe morbidity, mortality, operative time, intraoperative blood loss, harvested lymph nodes, and local recurrence rate.	Review only includes studies on low rectal cancer. A systematic review with subanalysis on low rectal cancers is included.
Ren J, Liu S, Luo H et al. (2021) Comparison of short-term efficacy of transanal total mesorectal excision and laparoscopic total mesorectal excision in low rectal cancer. Asian Journal of Surgery 44: 181–85	Non-randomised comparative study n=64	There were no statistically significant differences in the conversion rate, intraoperative complications, morbidity, serious morbidity, anastomotic leak, unplanned reoperation and hospital stay. The CRM distance in the TaTME group was longer than that in the LaTME group (6.8 mm versus 5.2 mm, p=0.039). The inter-group difference in terms of harvested lymph nodes, mesorectum integrity, CRM involvement, DRM distance, R1 resection, complete remission, pathological T stage, pathological N stage and pathological TNM stage was not statistically significant.	Studies with more patients or longer follow up are included.
Robertson RL, Karimuddin A, Phang T et al. (2021) Transanal versus conventional	Non-randomised comparative study (propensity	TaTME provided similar outcomes to conventional TME for rectal cancer with the application of IDEAL principles	Studies with more patients or longer follow up are included.

total mesorectal excision for rectal cancer using the IDEAL framework for implementation. BJS open 5 (no. 2)	score matched) n=218		
Roodbeen SX, De Lacy FB, Van Dieren S et al. (2019) Predictive factors and risk model for positive circumferential resection margin rate after transanal total mesorectal excision in 2653 patients with rectal cancer. Annals of Surgery 270: 884–91	Registry n=2,653	The incidence of positive CRM was 107 (4%). In multivariate logistic regression analysis, a positive CRM after TaTME was significantly associated with tumours located up to 1 cm from the anorectal junction, anterior tumours, cT4 tumours, extra-mural venous invasion and threatened or involved CRM on baseline MRI (ORs 2.09, 1.66, 1.93, 1.94, and 1.72, respectively).	Study focuses on identifying risk factors for positive CRM.
Roodbeen SX, Penna M, Mackenzie H et al. (2019) Transanal total mesorectal excision (TaTME) versus laparoscopic TME for MRI-defined low rectal cancer: a propensity score-matched analysis of oncological outcomes. Surgical Endoscopy 33: 2459–67	Non-randomised comparative study n=82	The resection margin was involved in 12% of patients in the laparoscopic group and 5% in the TaTME group (p=0.432). The TME specimen quality was complete in 84% of the laparoscopic cases and in 93% of the TaTME cases (p=0.266). Median distance to CRM was 5 mm in laparoscopic TME and 10 mm in TaTME (p=0.065). The conversion rate was 22% in the laparoscopic group, compared with none in the TaTME group (p<0.001). Other clinical outcomes did not show any statistically significant differences between the 2 groups.	Studies with more patients or longer follow up are included.
Rubinkiewicz M, Zarzycki P, Witowski J et al. (2019) Functional outcomes after resections for low rectal tumors: comparison of Transanal with laparoscopic Total	Non-randomised comparative study n=46	TaTME provided comparable outcomes in terms of functional outcomes in comparison to LaTME for TME in low rectal cancers. The prevalence of LARS was high and needs further evaluation of the technique.	Studies with more patients or longer follow up are included.

Mesorectal excision. BMC surgery 19: 79			
Rubinkiewicz M, Nowakowski M, Wierdak M et al. (2018) Transanal total mesorectal excision for low rectal cancer: A case-matched study comparing tatme versus standard laparoscopic TME. Cancer Management and Research 10: 5239–45	Non-randomised comparative study n=70	TaTME appears to be a noninferior alternative to laparoscopic surgery. TaTME allows for quality retrieval of surgical specimens with comparable clinical outcomes with laparoscopic TME.	Studies with more patients or longer follow up are included.
Rubinkiewicz M, Czerwinska A, Zarzycki P et al. (2018) Comparison of short-term clinical and pathological outcomes after transanal versus laparoscopic total mesorectal excision for low anterior rectal resection due to rectal cancer: A systematic review with meta-analysis. Journal of Clinical Medicine 7: 448	Systematic review n=778 (11 studies)	This meta-analysis shows benefits of TaTME technique for major postoperative complications. For clinicopathological features transanal approach is not superior to laparoscopic TME. Currently, the quality of the evidence on benefits of TaTME is low because of the lack of randomised controlled trials.	More recent systematic reviews are included.
Ryan OK, Ryan EJ, Creavin B et al. (2021) Surgical approach for rectal cancer: A network meta-analysis comparing open, laparoscopic, robotic and transanal TME approaches. European Journal of Surgical Oncology 47: 285–95	Network meta-analysis n=5,586 (178 TaTME)	While open TME was the most effective TME modality for short term histopathological resection quality, there was no difference in long-term oncologic outcomes. Minimally invasive approaches enhance postoperative recovery, at the cost of longer operating times. Technique selection should be based on individual tumour characteristics and patient expectations, as well as	Only 2 RCTs on TaTME were included.

		surgeon and institutional expertise.	
Shen Z, Yu G, Ren M et al. (2021) Multicenter investigation of bowel evacuation function after transanal total mesorectal excision for mid-low rectal cancer. International Journal of Colorectal Disease 36: 725–34	Case series n=361 follow up =median 12 months	The prevalence rate of no LARS, minor LARS, and major LARS in patients after taTME was 40%, 28%, and 32%, respectively. The 2 most frequently reported symptoms of LARS after taTME were bowel clustering (73%) and faecal urgency (63%).	Studies with more patients or longer follow up are included.
Shin JK, Kim HC, Yun SH et al. (2021) Comparison of transanal total mesorectal excision and robotic total mesorectal excision for low rectal cancer after neoadjuvant chemoradiotherapy. Surgical Endoscopy	Non-randomised comparative study n=306	Transanal and robotic TMEs have similar short-term outcomes for patients with rectal cancer after having neoadjuvant chemoradiotherapy.	Studies with more patients or longer follow up are included.
Shiraishi T, Ito M, Sasaki T et al (2020) Association between urinary function and resected pattern of the autonomic nerve system after transanal total mesorectal excision for rectal cancer. Colorectal Disease 23: 405–14	Case series n=231	The rate of urinary dysfunction was 12% at discharge. Multivariate analysis revealed that beyond TME and autonomic nerve system (ANS) resection were the 2 major independent risk factors for urinary dysfunction. Total ANS preservation had reduced rates of urinary dysfunction, and all patients were free from catheterisation 6 months after surgery. There was a higher rate of urinary dysfunction in total ANS resection than in partial ANS resection at 6 months after surgery.	Study focuses on association of urinary dysfunction and resected pattern of autonomic nerve system
Simillis C, Lal N, Thoukididou SN et al. (2018) Open versus laparoscopic versus robotic versus transanal	Systematic review n=6,237 (50 TaTME) 37 studies (29	The different techniques result in comparable perioperative morbidity and long-term survival. The laparoscopic and robotic approaches may improve postoperative	Only includes 1 RCT on TaTME.

mesorectal excision for rectal cancer: a systematic review and network meta-analysis. Annals of Surgery 270: 59–68	randomised controlled trials)	recovery, and the open and transanal approaches may improve oncological resection. Technique selection should be based on expected benefits by individual patient.	
Simillis C, Hompes R, Penna M et al. (2016) A systematic review of transanal total mesorectal excision: is this the future of rectal cancer surgery? Colorectal Disease: the official journal of the Association of Coloproctology of Great Britain and Ireland 18: 19–36	Systematic review n=510 (36 studies)	One death was reported, and the peri-operative morbidity rate was 35%. The anastomotic leakage rate was 6% and the reoperation rate was 4%. 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 CRM was negative in 95% of cases and the DRM was negative in 99.7%.	Only includes 1 RCT on TaTME. More recent systematic reviews are included.
Simo V, Tejedor P, Jimenez LM et al. (2021) Oncological safety of transanal total mesorectal excision (TaTME) for rectal cancer: mid-term results of a prospective multicentre study. Surgical Endoscopy 35: 1808–19	Case series n=173 follow up =median 23 months	A complete TME was achieved in 73%, while circumferential and distal margins were affected in 1.4 and 1.1%, respectively. Five patients developed local recurrences (3%) and 8% presented distant disease during the follow up. The 2-year disease-free survival and the overall survival rates were 88% and 95%, respectively.	Studies with more patients or longer follow up are included.
Simo V, Arredondo J, Hernan C et al. (2019) Rectal cancer treatment by transanal total mesorectal excision: Results in 100 consecutive patients. Cirugia Espanola 97: 510–16	Case series n=100 follow up =median 23 months	Laparoscopic TaTME is safe and effective with adequate circumferential and distal free margins and high quality of the resected mesorectum specimen. Post-operative morbidity is acceptable.	Studies with more patients or longer follow up are included.
Sparreboom CL, Komen N, Rizopoulos D et al. (2019) Transanal total mesorectal	Non-randomised comparative study n=96	The study showed that TaTME is a safe and feasible approach for rectal cancer resection. Postoperative	Studies with more patients or longer follow up are included.

excision: how are we doing so far? Colorectal Disease 21: 767–74		morbidity was similar to laparoscopic TME.	
Sylla P, Knol JJ, D'Andrea AP et al. (2019) Urethral injury and other urologic injuries during transanal total mesorectal excision: an international collaborative study. Annals of Surgery doi: 10.1097/SLA.0000000000003597	Case series n=39 injuries follow up =median 28 months	20 injuries happened during the teams' first 8 taTME cases ("early experience"). The urethral repair complication rate was 26% with a 9% rate of failed urethral repair needing permanent urinary diversion. In patients with successful repair, 18% reported persistent urinary dysfunction.	Study focuses on urological injuries.
van der Heijden JAG, Qaderi SM, Klarenbeek BR et al. (2021) Transanal total mesorectal excision and low anterior resection syndrome. The British Journal of Surgery	Non-randomised comparative study (propensity score matched) n=110	Higher LARS scores (30.6 versus 25.4, p=0.010) and more major LARS (65 versus 42%, p=0.013; OR 2.64, 95% CI 1.22 to 5.71) were reported after TaTME. Additionally, QoL score differences (body image, bowel frequency, and embarrassment) were worse in the TaTME group.	Studies with more patients or longer follow up are included.
van der Heijden JAG, Koeter T, Smits LJH et al. (2020) Functional complaints and quality of life after transanal total mesorectal excision: a meta-analysis. The British Journal of Surgery 107: 489–98	Systematic review n=846 (14 studies)	Meta-analysis found no statistically significant difference in major LARS between the 2 approaches (risk ratio 1.13, 95% CI 0.94 to 1.35, p=0.18). However, major heterogeneity was present in the studies together with poor reporting of functional baseline assessment.	A more recent systematic review is included.
van Oostendorp SE, Belgers HJ, Bootsma BT et al. (2020) Locoregional recurrences after transanal total mesorectal excision of rectal cancer	Case series n=266 follow up =median 24 months	The overall local recurrence rate in the implementation cohort was 10% (12/120), with a mean interval to recurrence of 15 months. Multifocal local recurrence was present in 8 patients. In the prolonged cohort (266 patients), the	Studies with more patients or longer follow up are included.

during implementation. British Journal of Surgery 107: 1211–20		overall recurrence rate was 6% (4% after excluding the first 10 procedures at each centre).	
Veltcamp H, Marloes K, Thomas WA et al (2019) Quality of life after rectal cancer surgery: differences between laparoscopic and transanal total mesorectal excision. Surgical Endoscopy 33: 79–87	Non-randomised comparative study n=54 follow up =at least 6.6 months	The EORTC-QLQ C30 and EQ-5D-3L questionnaires showed comparable outcomes in terms of quality of life between the 2 groups. Almost all items evaluated by the EORTC-QLQ C29, including sexual outcomes, were similar between the 2 groups. One item concerning faecal incontinence, was scored worse for TaTME. There were no statistically significant differences between the groups in terms of LARS symptoms or urinary function.	Studies with more patients or longer follow up are included.
Veltcamp Helbach M, Koedam T, Knol J et al. (2019). Residual mesorectum on postoperative magnetic resonance imaging following transanal total mesorectal excision (TaTME) and laparoscopic total mesorectal excision (LapTME) in rectal cancer. Surgical Endoscopy 33: 10.1007/s00464-018-6279-9.	Non-randomised comparative study n=64	Residual mesorectal tissue was detected in 3% of TaTME patients and of 47% in laparoscopic TME patients ($p<0.001$). Multivariate analysis identified only type of surgery as a significant risk factor for leaving residual mesorectum. Other known risk factors for incomplete TME, such as body mass index (BMI) and male gender, were not statistically significant.	Studies with more patients or longer follow up are included.
Veltcamp HM, van Oostendorp SE, Koedam TWA et al. (2019) Structured training pathway and proctoring; multicenter results of the implementation of transanal total mesorectal excision	Case series n=120	The first 10 patients in each centre were included for evaluation. Intraoperative complications occurred in 5% of patients. The clinicopathological outcome reported 100% for complete or nearly complete specimen, 100% negative DRM, and the CRM was positive in 5% of	Studies with more patients or longer follow up are included.

(TaTME) in the Netherlands. Surgical Endoscopy		patients. Overall postoperative complication rate was 45%, with 19% Clavien-Dindo 3 or higher and an anastomotic leak rate of 17%.	
Velthuis S, Nieuwenhuis DH, Ruijter TE et al. (2014) Transanal versus traditional laparoscopic total mesorectal excision for rectal carcinoma. Surg Endosc. doi:10.1007/s00464-014-3636-1	Non-randomised comparative study n=50	Within the transanal TME group, 96% of the specimens had a complete mesorectum, while in the traditional laparoscopic group, 72% was deemed complete ($p<0.05$). Other pathological characteristics, such as the CRM, were comparable between the groups.	Studies with more patients or longer follow up are included.
Vignali A, Elmore U, Milone M et al. (2019) Transanal total mesorectal excision (TaTME): current status and future perspectives. Updates in Surgery 71: 29–37	Review	Current studies show that TaTME has a low conversion rate, similar postoperative complications when compared with standard laparoscopic or open TME, excellent pathologic effectiveness and promising oncologic results. Nevertheless, some caution in the interpretation of the results is mandatory, since most of the published series come from highly trained surgeons in high-volume centres with results that are difficult to reproduce. In addition, some studies include the same patients in different reports and randomised trials on this issue are lacking.	No meta-analysis. More recent systematic reviews are included.
Wasmuth HH, Gachabayov M, Bergamaschi R et al. (2021) Statistical, clinical, methodological evaluation of local recurrence following transanal total mesorectal excision for rectal cancer: a systematic review. Diseases of the	Systematic review n=2,906 (29 studies)	The pooled rate of local recurrence was 3.4% (2.7% to 4.0%) at an average of 20 months with low statistical heterogeneity ($I2=0\%$). Meta-regression yielded no correlation between complete total mesorectal excision quality ($p=0.855$), circumferential resection margin ($p=0.268$), distal	Other systematic reviews with more outcomes have been included.

Colon and Rectum 899–914		margin (p=0.886), and local recurrence rates. Clinical and methodological heterogeneity were substantial. The evidence for or against transanal total mesorectal excision is inconclusive at this time.	
Wolthuis AM, Bislenghi G, de Buck van Overstraeten A et al. (2015) Transanal total mesorectal excision: Towards standardization of technique. World Journal of Gastroenterology 21: 12686–95	review n=323 (20 studies)	TaTME was associated with better TME specimens and a longer DRM. TaTME is feasible in expert hands, but the learning curve and safety profile are not well defined. Long-term follow up for anal function and oncological outcomes should be done in the future.	More recent systematic reviews are included.
Wu Z, Zhou W, Chen F et al. (2019) Short-term outcomes of transanal versus laparoscopic total mesorectal excision: A systematic review and meta-analysis of cohort studies. Journal of Cancer 10: 341–54	Systematic review n=751 (9 studies)	The meta-analysis suggested some advantages of TaTME, in terms of CRM involvement, operative time, blood loss, conversion, hospital stay, overall postoperative complications, and readmission. It appears that the TaTME procedure achieved a better resection quality and smoother recovery in selected patients, without compromising the short-term safety. It is too early to draw any conclusion because results of high-quality clinical evidence from randomised controlled trials have to be awaited.	More recent systematic reviews are included.
Xu C, Song HY, Han SL et al. (2017) Simple instruments facilitating achievement of transanal total mesorectal excision in male patients.	Case series n=115	Retrograde taTME with simple customised instruments can achieve high-quality TME, and it might be an effective and economical alternative for male patients with bulky tumours.	Studies with more patients or longer follow up are included.

World Journal of Gastroenterology 23: 5798–5808			
Xu W, Xu Z, Cheng H et al. (2016) Comparison of short-term clinical outcomes between transanal and laparoscopic total mesorectal excision for the treatment of mid and low rectal cancer: A meta-analysis. European Journal of Surgical Oncology 42: 1841–50	Systematic review n=466 (7 studies)	Compared with laparoscopic TME, TaTME is a feasible and safe approach for patients with mid and low rectal cancer. In addition, TaTME showed better short-term clinical outcomes, such as a longer CRM, lower risk of positive CRM, higher complete quality of TME rate, and shorter operative duration.	More recent systematic reviews are included.
Yamamoto S (2020) Comparison of the perioperative outcomes of laparoscopic surgery, robotic surgery, open surgery, and transanal total mesorectal excision for rectal cancer: An overview of systematic reviews. Annals of Gastroenterological Surgery 4: 628–34	review	The results suggest that all of the procedures have advantages and disadvantages, but that there are no decisive factors that could be used to select 1 procedure over any other. At the present time it cannot be demonstrated that laparoscopic surgery, robotic surgery, TaTME, or open surgery is superior to the other techniques, and it is important to select the best technique for each patient from among those that a surgeon can do.	The individual relevant systematic reviews have been included.
Ye J, Tian Y, Li F et al. (2020) Comparison of transanal total mesorectal excision (TaTME) versus laparoscopic TME for rectal cancer: A case matched study. European Journal of Surgical Oncology https://doi.org/10.1016/j.ejso.2020.11.131	Non-randomised comparative study n=140 follow up =median 18 months	There were no statistically significant differences between the 2 groups in terms of postoperative complications, conversion rate to open surgery and CRM. Local recurrence occurred in 2 patients (3%) in the transanal group, and 1 patient in the laparoscopic group (p=0.559). Kaplan-Meier survival analysis showed a 2-year local recurrence rate 1.5% versus 1.6%, disease-free survival 88% in both groups, overall	Studies with more patients or longer follow up are included.

		survival 94% versus 100% for transanal and laparoscopic group, respectively.	
Zeng Z, Liu Z, Huang L et al. (2020) Transanal total mesorectal excision in mid-low rectal cancer: evaluation of the learning curve and comparison of short-term results with standard laparoscopic TME. Diseases of the Colon and Rectum 64: 380–88	Non-randomised comparative study n=342 follow up =range 6 to 60 months	Short-term and histopathological outcomes are similar compared between transanal group and matched laparoscopic group. TaTME also provided good oncological outcomes.	Studies with more patients or longer follow up are included.
Zhang X, Gao Y, Dai XL et al. (2019) Short- and long-term outcomes of transanal versus laparoscopic total mesorectal excision for mid-to-low rectal cancer: a meta-analysis. Surgical Endoscopy 33: 972–85	Systematic review n=757 (11 studies)	Reports of TaTME indicated favourable outcomes considering mesorectal resection quality, CRM involvement, intraoperative blood loss, conversions, and postoperative complications, while the differences between the 2 groups had no statistical significance in terms of DRM, harvested lymph node, operation time, hospital stay, recurrence, 2-year overall survival and 2-year disease-free survival.	More recent systematic reviews are included.
Ziati J, Souadka A, Benkabbou A et al. (2021) Transanal total mesorectal excision for patients with rectal cancer: a systematic review and meta-analysis. The Gulf Journal of Oncology 1: 66–76	Systematic review n=2,542 (12 studies; 835 TaTME, 1,707 laparoscopic TME)	No statistically significant differences were seen in regard to positive circumferential resection margin, positive distal resection margin, macroscopic quality of mesorectum, and harvested lymph nodes. Concerning the perioperative outcomes, the results of conversion rates, operative time, hospital stay, anastomotic leakage and postoperative complications	Other systematic reviews with a later search date are included.

		were comparable between the 2 groups.	
Zuhdy M, Elmore U, Shams N et al. (2020) Transanal versus laparoscopic total mesorectal excision: a comparative prospective clinical trial from two centers. Journal of Laparoendoscopic & Advanced Surgical Techniques. 30: 769–76	Non-randomised comparative study n=38	TaTME enabled rectal cancer surgery in obese patients and increased the chance of transanal specimen extraction with equivalent oncological outcomes to conventional laparoscopic TME.	Studies with more patients or longer follow up are included.