



# Development of surgical concepts in rectal cancer resection and challenges in minimally invasive surgical proctectomy

Peadar S. Waters, Alexander G. Heriot

Division of Cancer Surgery, Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia

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*Correspondence to:* Mr. Peadar S. Waters. Division of Cancer Research, Peter MacCallum Cancer Centre, 305 Grattan St., Melbourne, Victoria, Australia. Email: peadarwaters@hotmail.com.

**Abstract:** Since the early 1900s there have been dramatic changes in the management of patients with rectal cancer. Surgical approaches initially performed for palliation, have now been adapted, modernised and undertaken as part of a multimodal approach. This has resulted in significant improvements in long-term oncological survival and patient quality of life. With the introduction of total mesorectal excision (TME) in the 1980's, and its global acceptance by the surgical community, local and distant disease-free survival in patients with rectal malignancy has significantly improved. Since the inception of minimally invasive surgery, laparoscopy has seen dramatic changes both in the evolution of technological advances and application in multiquadrant surgery for colorectal malignancy. Favorable short-term clinical benefits and long-term oncological equivalence from many multicentre randomized controlled trials in laparoscopic colonic cancer resection has led the colorectal surgical community to translate and adapt minimally invasive surgical (MIS) techniques for proctectomy in patients with rectal tumours. MIS proctectomy is technically challenging and is associated with a steep learning curve. Reported challenges in the literature continuously identify a group within three common themes which can be divided into patient/anatomical factors, tumour characteristics and the use of neoadjuvant therapies. Despite a large body of evidence highlighting efficacy of MIS in proctectomy, significant challenges exist in male patients with a narrow pelvis and distal tumors. Such patients are at increased risk of a poor surgical specimen, positive distal and circumferential resection margins (CRMs), and increased local recurrence. Despite advances in laparoscopy and robotic platforms, approaching such lesions from a “top down” approach expose the ongoing limitations to lower pelvic access. This technically challenging issue has led to the colorectal surgical community adopting previously taught MIS techniques to develop a “bottom up” transanal approach to TME, now known as transanal TME (taTME) in order to mitigate this increased margin risk.

**Keywords:** Total mesorectal excision (TME); minimally invasive surgery; rectal cancer; proctectomy; transanal TME (taTME)

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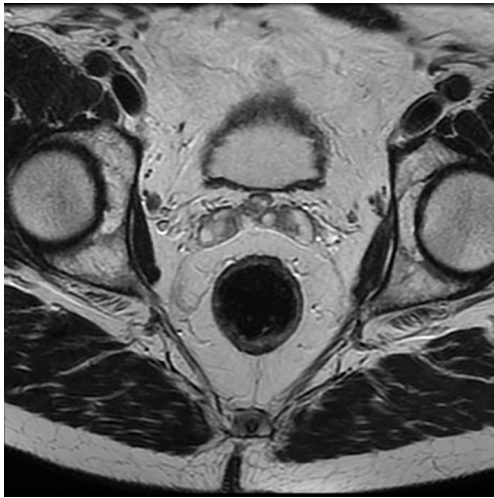
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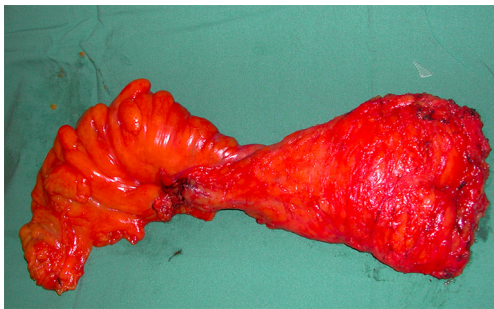
## Introduction

Surgery continues to remain the cornerstone for curative intent in patients with rectal cancer. Despite reporting significant oncological improvements with multimodal therapies such as chemoradiotherapy in the neoadjuvant

and adjuvant setting, all patients, except for complete responders, continue to undergo some form of operative intervention for definitive management (1,2). Such operative intervention ranges from local excision to a restorative or non-restorative proctectomy with total



**Figure 1** Axial pelvic MRI delineating the TME plane (red line) of embryological origin resulting in *en bloc* resection of the rectum with the surrounding mesorectum (draining blood vessels and lymphatics).



**Figure 2** Resected specimen showing an intact good quality complete mesorectal incision in a patient with a distal rectal tumour undergoing a laparoscopic ultralow anterior resection.

mesorectal excision (TME). The history and evolution of rectal cancer surgery is an incredibly interesting one that spans throughout the last century with a change of focus from palliation to curative intent with improved patient and long-term oncological outcomes. Miles performed the first rectal resection with radicality for curative intent in 1907 in which he performed an abdominoperineal resection (APR) in a patient with a rectal malignancy. Miles APR became the gold standard for many decades (3). Earlier reports however do exist by Czerny [1884] and Mayo [1904] highlighting the use of a combined abdominal and perineal approach to facilitate proctectomy (4,5). During this time period it was assumed that rectal malignancy metastasised both

proximally and distally in a tubular fashion and therefore distal control in the form of a complete proctectomy and end colostomy formation was necessary in all patients (6).

Overtime, with the development of surgical adjuncts such as leg stirrups, pelvic retractors, surgical stapling devices in tandem with a greater understanding of rectal cancer biology there has been dramatic changes in both the surgical approach and management of patients with rectal cancer. After Miles had noted recurrence of tumor in the pelvic mesocolon in the 1890's, Sir Berkeley George Andrew Moynihan postulated in the 1920s that surgical resection of a malignant organ should not be confined to the organ, however, should encompass the synchronous resection of the surrounding lymphatic system (7). Further changes in surgical approaches were observed in France in 1921 when Henri Albert Hartmann performed an anterior resection for proximal rectal tumours with preservation of the sphincter complex and thus reducing the morbidity and mortality associated with a perineal resection (8). In the post World WarII era, further advances were achieved in performing restorative resections. Dixon in 1948 reported the first series demonstrating favourable outcomes from the Mayo Clinic in patients undergoing anterior resection with restoration of GI continuity (9). Anterior rectal resections significantly increased with improved development and broader accessibility to surgical stapling devices. The capabilities of sphincter preserving resection with low anastomosis was further aided in 1983, when Pollett *et al.* demonstrated that a 2 cm distal resection margin did not alter long-term survival compared to the previous proposed 5 cm "safety margin" (10). Throughout the 1980's multiple studies were published, documenting the ability to achieve restoration with adequate functional outcomes in distal rectal cancers by undertaking a coloanal or intersphincteric anastomosis with or without pouch formation (11).

Of late, one of the greatest advances in modern rectal cancer management has been the introduction of TME by Heald in 1982. TME is now recognised throughout the literature as standard of care for the surgical approach in patients with rectal tumours (12). TME, involves meticulous dissection along the non-vascular TME plane of embryological origin resulting in *en bloc* resection of the rectum with the surrounding mesorectum (draining blood vessels and lymphatics, *Figure 1*) (13). Prior to this technique, anterior resections were typically performed with blunt dissection of the rectal tube in the mid and distal one third resulting in high local recurrence rates (>20%) and overall 5-year survival less than 50% (14).

## Principles of rectal cancer surgery

The basic principles for rectal cancer surgery are the division of the major vascular pedicle (inferior mesenteric artery, IMA) supplying the rectum along with its lymphatics, obtaining a tumour free circumferential resection margin (CRM) and *en-bloc* resection of any contiguous organs or structures attached to the tumour. This should be performed meticulously, preserving the autonomic nerve plexus where not involved (*Figure 2*). Additionally, macroscopic evaluation should demonstrate a smooth mesorectum without defects. Complete TME is associated with lower rates of local recurrence (15-17). Despite maximum efforts, TME is technically difficult due to myriad of patient, tumour, and treatment factors, resulting in sub-optimal resection. Factors such as a narrow male pelvis, obesity, locally advanced mid, distal and anterior rectal tumours and post-radiotherapy treatment are well established as adversely affecting margin clearance. This has led to the development and application of a modified transanal approach to rectal cancers in high volume centres (18-23). During initial studies examining pathological margin clearance, distal and proximal margins were initially reported rather than CRM. After initial concepts of proximal and distal tumour extension were clarified, Golligher *et al.* reported data highlighting that local tumour dissemination did not exceed 2 cm from the distal margin in 98% of 1,500 analysed rectal specimens (24). Two decades later it has been further demonstrated a distal tumour margin of >1 cm confers no oncologic superiority (11,25). More recently, authors have documented that patients undergoing sphincter preserving surgery with intersphincteric dissection and neoadjuvant chemoradiation with margins of less than 1 cm are not compromised from a local recurrence or overall disease-free survival (26).

Obtaining a complete mesorectal excision confers significantly improved local recurrence rates. High recurrence rates are seen in patients with an incomplete mesorectal excision and this was previously reported as high as 25% for stage 2 and 3 rectal adenocarcinomas managed with surgery alone (27). By resecting the mesorectum, this theoretically encapsulates the distal extramural spread and CRM of excision thus allowing for an R0 resection. Within the Dutch mesorectal trial, local recurrence was reduced to 8.2% by performing a complete surgical TME alone (28).

It has now been widely recognised that radial or CRM is of significant prognostic benefit. CRM is defined as the non-peritonealised surface of a resected specimen created

by the dissection of the subperitoneal aspect at surgery (29). An involved CRM has been shown to be associated with increased rates of both local and distant disease and is typically a marker of the quality of surgery performed (30-33). The pathological assessment of the mesorectal plane is also an important measure of the quality of the surgical resection. Most studies consider a CRM as positive when it is <1 mm from the tumour margin (34,35). Patients undergoing APR compared to low anterior resections have been documented to have increased rates of positive CRM with approximately 16% of patients developing local recurrence within two years of surgery (36). Moreover, patients with a CRM of greater than 2 mm had a significantly lower local recurrence rate. When examining distant metastatic disease, patients with a positive CRM developed metastatic disease in 37.6% of cases as opposed to 12.7% in those with a CRM >1 cm.

Other key principles in proctectomy is restoration of gut continuity and autonomic nerve function preservation while achieving oncological cure where possible. Surgical exposure and precise dissection of the TME plane with effort to correctly identify and preserve pelvic autonomic nerves is paramount in proctectomy. Multiple factors including poor visualisation, bulky tumours, post neoadjuvant therapy and pelvic morphology can hinder precise dissection and result in increased incidence of urinary and sexual dysfunction (37). Anatomically the rectum descends concavely along the sacrum and is confined within a rigid fixed space bounded by the ischial tuberosity and iliac wings laterally and pubic symphysis anteriorly. In a select group of patients with a narrow or deep pelvis adherence to the principles of proctectomy and TME surgery can be very challenging even in the hands of experience colorectal surgeons. A study analysing sexual dysfunction following rectal cancer surgery in both male and female patients using a survey style questionnaire reported that 76% of patients experienced moderate to severe sexual dysfunction after rectal cancer treatment (38). Similarly, Dulskas *et al.* reported that erectile dysfunction rates in males increased from 41.7% in the pre-operative setting to 63.9% post-operatively with sexual dysfunction increasing from 83.3% to 94% post-operatively in females (39). Moreover, urinary dysfunction significantly increased from 80.1% to 88.9% in male patients. With greater understanding of pelvic anatomy and increased survivorship in patients undergoing proctectomy is it critical that every adjunct possible is utilised to improved rectal dissection and nerve preservation. A recent study by Attaallah *et al.* in 2018 highlighted a significantly lower

rate of sexual dysfunction in both male and female patients undergoing laparoscopic proctectomy compared to open proctectomy (40). Oncology safety in conjunction with well described patient benefits have translated to increasing rates of minimally invasive surgical (MIS) approaches to rectal cancer in the last two decades (41-45).

### Benefits of MIS

To date, numerous studies have demonstrated clear advantages of laparoscopic over open surgical colorectal resection (46,47). Advances in laparoscopic surgery since the 1990s has been one of the greatest milestones in the technical evolution of medicine. Notes dating as far back as Hippocrates (460–375 B.C.) documented the use of placing instruments into natural human orifices to inspect internal anatomy. Major advances in laparoscopy occurred after the invention of the lightbulb by Edison in 1879 which saw the development of a rigid endoscopic device with an inbuilt light source (48). Kelling and Ott have been credited with performing the first true laparoscopic procedure by utilising an incision in the posterior vaginal fornix to advance a “ventroscope” to examine the pelvic cavity (49). With the development of new equipment and the use of carbon dioxide for insufflation a German surgeon known as Kurt Semm performed the first appendectomy in 1982 and Erich Muehe undertook the first successful laparoscopic cholecystectomy in 1985 (50). Prior to 1991 all laparoscopic surgeries were confined to a single quadrant until Jacobs *et al.* performed the first multiquadrant laparoscopic assisted colectomy (51). Despite initial concerns surrounding high rates port site metastases which were subsequently refuted, cases of laparoscopic surgery excelled and a large number of trials were undertaken to examine oncological outcomes in laparoscopic colorectal resection. Multiple randomised controlled trials (RCTs) such as COST 2004, MRC CLASiCC 2005, COLOR 2009, and ALCCAS 2010 in laparoscopic colonic surgery have consistently demonstrated the safety and oncological equivalence to open resection (45,52-56). The COST study reported outcomes on 872 randomised cases from 1994–1999 across 48 institutions by video credentialed surgeons with a 4.4 years mean follow-up. No significance difference in survival between patients undergoing open versus laparoscopic colectomy for stage 1–3 disease was seen. Following a decade of multicentre trials and a large number of publish meta-analyses, laparoscopic colonic resection has now been widely accepted by the colorectal community as equivalent

in long-term oncological outcomes with significant short-term benefits over open surgery (57). Most notably laparoscopic interventions have been shown to be associated with reduced blood loss, early feeding, faster recovery, lower morbidity, shorter length of hospital stay and decreased hernia rates (46,47). With such positive early clinical and long-term oncological outcomes laparoscopic intervention for malignancy was translated to rectal cancer resection (58).

### MIS proctectomy

Technological advances in minimally invasive proctectomy has significantly progressed in the last decade. The development of 3D laparoscopes with higher degrees of instrument versatility and greatly improved adjuncts such as laparoscopic fluid suction devices, retractors and staplers has led to an increased number of centres now performing proctectomy for both benign and malignant diseases laparoscopically. This has and undoubtedly continues to divide colorectal surgeon opinion on best approach to proctectomy particularly in the setting of rectal malignancy. Supporters of open proctectomy state that regardless of the short-term benefits, a laparoscopic approach may not allow the same oncological clearance and adequate TME resection. Multiple publications including multicentre trials have demonstrated Laparoscopic TME to be equivalent or superior to open TME (*Table 1*) (59,60). To date there have been some inherent weaknesses to the published studies surrounding MIS proctectomy. A large proportion of data comes from non-randomised comparative studies commonly reporting outcomes on both colonic and rectal cancers. Therefore, a large degree of heterogeneity exists in earlier MIS proctectomy studies. Early experience by Morino *et al.* in 2003 reported outcomes in 100 consecutive resections for mid/low rectal cancers (average 6.1 cm from anal verge) (61). Mean operative time was 250 minutes with a 12% conversion rate and 12-day hospital stays. Local recurrence and survival at four years was 4.2% and 82% respectively. Since then numerous studies have reported favourable outcomes in MIS proctectomy (*Table 1*).

A large multicenter randomized controlled trial, COLOR II, analysed 3-year locoregional recurrence and survival in 1,044 patients undergoing laparoscopic and open resection for rectal cancer (62). Their findings reported equivalent locoregional recurrence and disease free and overall survival in patients undergoing MIS proctectomy compared to open. Most recently in 2019 the ACOSOG Z6051 study from the United States reported disease free survival and recurrence

**Table 1** Studies reporting outcomes in MIS proctectomy

Title/primary author, year (country of origin) (patient number)
• Hong Kong 2000 [34]
• CLASICC (Singapore) 2001 [236]
• Araujo (Brazil) 2003 [28]
• Hong Kong 2003 [40]
• Zhou (China) 2004 [171]
• Hong Kong 2004 [403]
• CLASICC (UK) 2005 (381 rectal)
• King (UK) 2006 [62]
• Braga (Italy) 2007 [168]
• Pechlivanides (Greece) 2007 [73]
• Zhou (China) 2007 [71]
• Ng (China) 2008 [99]
• Lujan (Spain) 2009 [204]
• Hong Kong 2009 [153]
• Kang (Korea) 2010 [340]
• Liu (China) 2010 [186]
• COLOR II b 2011 [40]
• Liang (China) 2011 [343]
• COLOR II a 2013 [1,044]
• COREAN (Korea) 2014 [340]
• ALaCaRT (Australasia) 2015 [475]
• ROLARR (UK) 2017 [471]
• Z6051 (USA) 2019 [462]

MIS, minimally invasive surgical.

in 462 patients undergoing open and laparoscopic rectal resection for cancer (63). They concluded that there was no significant difference in oncological outcomes in both groups. Finally, a study from Japan concentrating on low rectal tumours examined laparoscopy compared to open resection in advanced low rectal tumours in 1,500 patients across 69 institutions (64). Hida *et al.* reported significantly less complications in the laparoscopic group with no difference in recurrence-free survival and overall survival at three years. Despite the majority of studies reporting oncological equivalence in MIS proctectomy compared to open, concerns do exist regarding a lack of pathological equivalence (Z6051 & ALaCaRT) and distal rectal cancer

resection remains technically challenging.

### Challenges of MIS rectal resection

Despite improvement in minimally invasive techniques to proctectomy, access to distal 1/3 tumors, especially in male, obese patients, remains technically challenging. Neoadjuvant chemoradiotherapy, in conjunction with local tumor edema or fibrosis, can further complicate plane identification and dissection. This results in an increased risk of margin positivity, reduced distal resection margin and an incomplete (grade 1) mesorectal specimen, associated with increased local recurrence rates and suboptimal long-term disease free and overall survival. Warriar *et al.* reported that low rectal cancers were an independent risk factor for CRM positivity (65). Moreover Daniel *et al.* documented significantly reduced survival rates in rectal cancer patients with obesity (66). Interestingly however a meta-analysis in 2016 focusing on surgical outcomes in obese and non-obese patients highlighted that obese patients had significantly increased rates of conversion to open and post-operative morbidity without significant influence on pathological results (67). Despite this, the importance of achieving a good quality TME with negative margins is paramount to patient outcome. Due to tapering of the rectal wall and mesorectal fascia as the low rectum descends towards the anus the range for error reduces and risk of a positive margin increases. Due to fixed trocar placement and reduced angulation in a fixed bony pelvis visualisation and determination of the distal margin can often be imprecise leading to high conversion rates of up to 34% (45). A pioneering approach to overcome these non-modifiable factors has been developed and currently utilised globally. Transanal TME (taTME), or “bottom up” approach to rectal cancer overcomes many of the described hindrances to access and precise dissection of the distal rectum, translating to improved pathologic specimens in early global registries (68).

### Conclusions

The management of rectal cancer has seen dramatic changes over the last century. Multimodal treatment is now the mainstay in managing such patients. Minimally invasive surgery has continued to evolve and has now revolutionised our approach to patients with rectal cancer. MIS proctectomy has clearly become a core technique in the armamentarium of colorectal surgeons performing

TME surgery. This inclusion was initially due to promising data from multicentre randomised controlled trials in MIS colonic resection for malignancy. In the last decade numerous studies have reported oncological equivalence in MIS proctectomy compared to open resection with significant short-term patient benefits. Despite this MIS proctectomy for distal rectal tumours can be challenging in obese male patients with large bulky distal tumours in a fixed narrow bony pelvis. The literature has continuously highlighted that such patients are at increased risk of margin positivity with subsequent increase local recurrence and poor overall survival rates. A pioneering approach called taTME has been developed to overcome these non-modifiable factors by performing a “bottom-up” TME dissection, with promising early results.

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