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REVIEW

Recent advances in the management of rectal cancer: No surgery, minimal surgery or minimally invasive surgery

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Abstract

Over the last decade, with the acceptance of the need for improvements in the outcome of patients affected with rectal cancer, there has been a significant increase in the literature regarding treatment options available to patients affected by this disease. That treatment related decisions should be made at a high volume multidisciplinary tumor board, after pre-operative rectal magnetic resonance imaging and the importance of total mesorectal excision (TME) are accepted standard of care. More controversial is the emerging role for watchful waiting rather than radical surgery in complete pathologic responders, which may be appropriate in 20% of patients. Patients with early T1 rectal cancers and favorable pathologic features can be cured with local excision only, with transanal minimal invasive surgery (TAMIS) because of its versatility and almost universal availability of the necessary equipment and skillset in the average laparoscopic surgeon, emerging as the leading option. Recent trials have raised concerns about the oncologic outcomes of the standard "top-down" TME hence transanal TME (TaTME "bottom-up") approach has gained popularity as an alternative. The challenges are many, with a dearth of evidence of the oncologic superiority in the long-term for any given option. However, this review highlights recent advances in the role of chemoradiation only for complete pathologic responders, TAMIS for highly selected early rectal cancer patients and TaTME as options to improve cure rates whilst maintaining quality of life in these patients, while we await the results of further definitive trials being currently conducted.

Key words: Rectal cancer; Watchful waiting; Transanal minimal invasive surgery; Transanal total mesorectal excision

Core tip: Over the last decade several additional surgical

options have become available in the management of rectal cancer. These extend from non-surgical management with chemoradiation only, local excision for selected cases of early rectal cancer and the standard total mesorectal excision but now by a transanal approach. Although long-term outcome studies are ongoing, it is the duty of the multidisciplinary team treating these patients to be familiar with these options, as they may be of benefit to selected patients with this disease.

Plummer JM, Leake PA, Albert MR. Recent advances in the management of rectal cancer: No surgery, minimal surgery or minimally invasive surgery. *World J Gastrointest Surg* 2017; 9(6): 139-148 Available from: URL: http://www.wjgnet.com/1948-9366/full/v9/i6/139.htm DOI: http://dx.doi.org/10.4240/wjgs.v9.i6.139

INTRODUCTION

Colorectal cancer (CRC) is the third most common cancer affecting males and females in most western countries and is a leading cause of cancer related deaths with rectal cancer accounting for up 40000 of these new cases in the United States[1]. Rectal cancer is more common in men and until recently compared to cancer in the more proximal large intestines mid and lower rectal cancer was traditionally associated with higher rates of local recurrence and reduced disease free survival[2]. In addition curative surgery is associated with higher risk of morbidity and greater long-term consequences, including a poorer quality of life compared to colon cancer surgery. Up to 40% of affected patients are treated with a permanent stoma especially when performed by general surgeons[3].

Over the last few decades significant strides have been made in the treatment of rectal cancer with the adherence to strict anatomical dissection as popularized by Heald *et al*[4], the recognition of the importance of neoadjuvant therapy in reducing local recurrence rates as led by the Swedish and Dutch trials[5,6], and the fusion of surgery with technology in effecting minimally invasive surgery being the most critical. The various European structured intervention programs have all led to a reduction in local recurrence rates, lower permanent stoma rates and higher cure rates[7-9]. The acceptance of the need for similar interventions in the United States and hopefully its benefits has since led to the introduction of initiatives such as the OSTRiCh[10,11] and its National Accreditation Program for Rectal Cancer (NAPRC) that was established jointly with the Commission on Cancer and adopted as a quality program by the American College of Surgeons[12]. This program's goal is to ensure that all (> 95%) of rectal cancer patients receive appropriate individualized evidence-based care using a multidisciplinary team of qualified doctors, and offering appropriate magnetic resonance imaging (MRI) based staging, detailed pathologic assessment and delivering quality TME, whilst tracking adherence to these standards and patient outcome. The net effect is that more rectal cancer patients will receive their high quality care in fewer centers that will be advantageous for recruitment into clinical trials to address current areas of uncertainty.

The introduction of laparoscopic colonic surgery for malignant disease has been supported by good level evidence of short-term benefits to patients without compromising oncologic outcome[13-15], but this can not be said to be the same with mid and low rectal cancer surgery. While the short-term indicators may be superior, various studies[15,16], have not always supported equivalence in oncologic outcomes with high circumferential resection margin (CRM) positivity being an initial concern. As such, patients undergoing surgery for rectal cancer must be informed of all treatment options and preferably be treated in a high volume center.

Difficulty with rectal cancer surgery is especially evident in the narrow male pelvis, and given that obesity is now endemic, the bulky mesorectum that must be excised completely for mid and low rectal cancers often pose challenges laparoscopically, when done in the usual "top-down" manner. The importance of a detailed pathologic report to inform quality of surgery [grade of the total mesorectal excision (TME)] and adjuvant therapy (degree of differentiation and lymphovascular invasion in addition to nodal status) has also been recognized in recent times, as is appropriate local preoperative staging with pelvic MRI. Modern high-resolution MRI techniques can accurately predict depth of spread within 1mm of histopathology assessment and therefore predicting the likelihood of a clear CRM[17,18], and unlike endorectal ultrasound (ERUS), it can identify nodal disease in the entire mesorectum and the pelvic side-wall compartment[19] which are markers of local recurrence and overall survival. Nowadays, MRI and ERUS are complementary and when used simultaneously, will result in a significant increase of the overall accuracy for the T stage of the rectal cancer[20].

In the last decade, three innovations of the surgical care of rectal cancer care have been introduced with the potential to revolutionalize the treatment of rectal cancer patients. These are watchful waiting after neoadjuvant chemoradiotherapy for complete pathologic responders, that is, no surgery or primary treatment (by default) with chemoradiotherapy, transanal minimally invasive surgery (TAMIS), minimal surgery, and transanal total mesorectal excision (TaTME) the latest version of minimally invasive surgery. They are promising options that in the appropriately selected patient have a role as we strive to optimize cure rates whilst maintaining optimal quality of life in the individuals affected by this disease. In addition to the evolution of surgical techniques, the continued standardization of therapy as determined in a multidisciplinary tumor board (MDT) has lead to the practice of more evidence-based medicine applied to rectal cancer management to the benefit of patients. While the role of the MDT will not be addressed further in this

review it is fair to say that compared to a single surgeon management, better decisions are more likely to be made and the patients are more likely to complete all aspects of their therapy, thus achieving the mandate of the NAPRC.

NO SURGERY

Preoperative local staging with a rectal MRI is mandatory in all patients with a diagnosis of rectal cancer, complemented by ERUS especially in the evaluation of early rectal lesions, where it may be superior to MRI[20]. The performance of ERUS is operator dependent and limited in the presence of a stricture[20]. Therefore the determination of tumour thickness, the precise mesorectal fascial margin, the presence of extramural venous invasion provided by MRI facilitate patient selection for neoadjuvant chemoradiotherapy in an attempt to reduce local recurrence rates. Following neoadjuvant chemoradiotherapy, patients have traditionally proceeded to radical surgery with TME (APR or LAR) in the following 6-12 wk. With refinements in chemoradiotherapy approximately 10%-30% of rectal cancer patients who receive neoadjuvant chemoradiotherapy demonstrate complete resolution of their tumor on final pathologic evaluation, pathologic complete responders (pCR). Patients treated with TME after achieving ypT0 status have local recurrence rates of less than 1% and 5-year survival rates of more than 95%[21]. All other options must be comparable to this standard with respect to cancer survival.

Led by the persistence of Habr-Gama *et al*[22], it has been demonstrated that following long-course neoadjuvant chemoradiotherapy, patients with a complete clinical response can be managed by "watchful-waiting" rather than radical resection[23-26]. This is especially attractive in elderly patients, those with excessive comorbidities and for patients whose curative surgery may require a permanent stoma. One must also carefully consider the significant gastroenterologic, sexual and urologic functional outcomes associated with radical surgery which alter quality of life, as we know that poor functional outcome is more likely in patients receiving radiotherapy and radical resection[26-28].

Patients are treated with 1.8-2.0 Gy in 25 daily fractions to a total of 45-50 Gy and given concurrently with fluropyrimidine-based chemotherapy. Extended dose of chemoradiation therapy with additional chemotherapy cycles and 54 Gy of radiation may result in higher (> 50%) sustained complete clinical response rates that may ultimately avoid radical resections[29]. Assessment of response to neoadjuvant chemoradiotherapy is ideally done initially 8-10 wk after completion of chemoradiotherapy. A pale, white scar including telangiectasiss, along with the absence of ulceration or any mucosal abnormality is considered a complete clinical response[29]. The use of the previous strict diagnostic criteria remains challenging and repeatedly has demonstrated underestimating the number of complete pathologic responders secondary to persistent mucosal irregularities at the initial cancer site[30]. This has led many to extend the period of observation prior to surgery outward of 20 wk. On the contrary, approximately 25% of patients determined to have a complete clinical response ultimately develop tumor regrowth within one year. Radiological restaging is often utilized but not sensitive or specific because of the post-treatment changes making interpretation difficult. Improvements in radiologic technique and modality should continue to resolve this troublesome problem while the finding of minimal radiological response should prevent undue delays to radical resection.

Residual mucosal abnormality is predictive of luminal recurrence and should be carefully documented and biopsied. Coupled with clinical examination, endoscopic assessment and biopsy has been shown to possess a false negative rate of 69%[31]. ERUS has a low specificity 33% for luminal disease but has a 81% negative predictive value for lymph node involvement[31]. Like pre-treatment staging, MRI has been named the gold standard post neoadjuvant therapy[32]. The use of T2 weighted MRI may have an accuracy of 92% in identifying complete responders in terms of local disease but it has a tendency to over stage nodal spread[32]. The use of MRI diffusion weighted imaging has become a superior technique to evaluate tumor resolution and fibrosis. While it may be superior to ERUS for advanced T stages, in a recent meta-analysis looking specifically at T0 disease it showed 19% sensitivity and 94% specificity[33].

In the largest meta-analysis to date involving 2224 patient, de Jong *et al*[34] concluded radiological evaluation by ERUS, MRI and CT, while still performed, have a poor accuracy at predicting complete tumor response and the accuracy of these modalities to predict the presence of metastatic lymph node disease is also low. This has led to the investigation of various tools such as magnetic resonance tumor regression grade-which is reportedly 10 times better than clinical assessment in identifying complete responders)[29]. This tool needs further validation and for now these investigations cannot be used in isolation to accurately predict response to therapy, but rather they have to be taken in context of the overall assessment.

Watchful-waiting as primary treatment for rectal cancer requires meticulous follow-up. In the first year patients are seen at one to three-months intervals for clinical examination and this must include digital and endoscopic rectal examination. Patients with a sustained cCR after one year will have continued surveillance every three months for an additional year and every six months thereafter[22-24]. Various local and systemic radiological investigations are performed at 3-6 mo intervals for 5 years. A positive result mandates crossover to radical resection. The majority of patients who develop non-metastatic local re-growth can undergo salvage surgery without adversely affecting their survival[35]. In the meta-analysis by Li *et al*[36], while patients treated with watchful-waiting had an increased risk of local recurrence compared to radical resections these patients had similar overall survival at 1, 2, 3 and 5 years after their diagnosis and treatment once they receive appropriate follow-up and timely intervention when indicated.

Table 1 Publications of "no surgery" for rectal cancer including minimum 20 patients in their study (2006-2016)

Ref.	No. of patients	Local recurrence (%)	Systemic recurrence	%undergoing salvage surgery	Disease free survival	Overall survival %
Habr-Gama *et al*[23]	90 (183)	28/90	14%	93	68	91 at 5 yr
Maas *et al*[24]	21	1/21	0	100	93	91 at 2 yr
Smith *et al*[25]	32	6/32	3/32	NA	88	96 at 2 yr
Araujo *et al*[26]	42	5/42	7/42	80	60.9	71.6 at 5 yr
Renehan *et al*[35]	129	44/129	3	36/41	88	96 at 3 yr

NA: Not reported.

There are several areas of uncertainty regarding this management approach. These include optimal timing and best method of assessment of response to therapy, the role of extended chemoradiation, standardization of follow-up to detect recurrences early for the best outcome and the role of further local resection *vs* radical surgery for salvage of failures. The reports of success with this management approach are from a few highly specialized centers (Table 1). Review of the literature will show that the patient numbers are small relative to the burden of the disease and outcome, albeit limited follow-up in most series, is not as good as if the patients were treated with radical resection. It is fair to say that while there is a role for this line of management in up to 20% of rectal cancer patients, they must be fully informed about the possible need for radical resection and it all should be done whilst adhering to a strict protocol.

MINIMAL SURGERY

Increasingly patients with CRC are being diagnosed on screening colonoscopies and at an earlier stage with localized disease being the most common stage at presentation[37] both in the United States and worldwide[38]. The number of patients diagnosed with localized rectal cancer has increased over the last three decades with localized rectal cancer being more commonly diagnosed than localized colon cancer[39]. There is also greater understanding of tumor biology and other harbingers of biologically aggressive disease. With this comes the acceptance that there may be a role for less radical surgery in patients with early rectal cancer and good prognostic features such as the absence of lymphovascular invasion. Favorable T1 cancers have less than a 10% chance of having lymph node metastasis[40,41] and complete local excision only can be curative. Early rectal cancer is defined as rectal cancer confined to the submucosa[42] and is subdivided by Kikuchi *et al*[43] based on the depth of invasion into: sm1: Slight submucosal invasion from the muscularis mucosa (upper 1/3); sm2: Intermediate (middle 1/3) invasion; and sm3: Carcinoma near the inner surface of the muscularis propria (lower 1/3).

There are several acceptable local options to treat early rectal cancer including transanal excision (TAE), transanal endoscopic microsurgery (TEM) and TAMIS. They all avoid the consequences of radical excision of the rectum but also have the disadvantages of the need for increase vigilance after treatment and greater local failure rates even in appropriately selected patients. TAE and TEM have both been available options before TAMIS was described by Atallah *et al*[44] but compared to TAE, TAMIS carries the advantages of wider application to lesions further away from the anal verge and with less fragmentation[45], while the use of a flexible laparoscopic platform gives it benefits of reduced capital expenditure for equipment acquisition and less post-procedural sphincteric complications compared to TEM[46,47]. TAMIS therefore has distinct advantages above its competitors and since its introduction its use has grown exponentially[48]. Local excision with an advanced platform should be an option in the care of all patients with early rectal cancer patients. While some patients having local recurrence can undergo salvage radical resection without any reduction in expected survival[45,49], some patients may not be as fortunate[50]. Data from patients undergoing TEM and followed by radical resection show a reduction in the quality of the TME performed when compared to similar patients treated by TME alone[45]. Poor quality TME leads to increase local recurrence and a reduction in survival, emphasizing the importance of patient selection as an important determinant of outcome from local excision.

The patients undergoing TAMIS are placed in lithotomy position and the operative monitor is placed at the patient's head. Basic laparoscopic instrument required are a long 5 mm angled camera, a grasper, eletrocautery, needle drivers and one of two Food and Drug Administration approved ports for TAMIS[47] (SILS Port and the GelPOINT Path). A good suction device is important for smoke evacuation such as the recently introduced insufflators like AirSeal Insufflation System which provide improved stability of pneumorectum at lower pressures and reduced intraluminal smoke.

The procedure begins with the marking out of the lesion with at least a 1 cm margin in all directions using eletrocautery. Care must be taken to ensure a full thickness division of the rectal wall without coning by dissecting perpendicular to the rectal wall until the mesorectal fat entered. The majority of the dissection is done with eletrocautery and during excision and manipulation the specimen must be grasped on the edge of normal mucosa to prevent fragmentation of the tissue. Particular attention

must be taken for anterior lesions as to avoid injury to the urethra, prostate, or vagina. The resected specimen must be appropriately oriented, pinned and labeled for adequate pathological evaluation and reporting.

Adequate hemostasis is obtained before closing the rectal wall defect and in fact best method of handling the defect is debatable. There is evidence that defects of the extraperitoneal rectum do not have to be closed if they are in a posterior location and these have little consequence[51]. If the decision is to close the defect this is done transversely so as not to narrow the lumen significantly. Sigmoidoscopy can be done at the end of the procedure so as to assess the luminal diameter if there are any concerns.

Patients are usually fed once they have recovered from anaesthesia and there are no dietary restrictions. Post-operative pain is negligible and most patients are discharged after one night in hospital. The frequency of clinical review maybe institution based but there is general agreement that the patients are seen once the histology of the resected specimen is available for a full discussion. In the event that the patients were upstaged after TAMIS (sm3 with high-grade histologic features or more advanced disease on the final resected histology), these patients must be offered the ideal option of a more radical resection involving TME. This may take the form of an anterior or abdominoperineal resection[44]. Repeat TAMIS is also an option for patients with T1 disease and a positive margin microscopically. Some patients may opt for treatment with adjuvant radiotherapy[52]. There is no consensus about the timing of the radical surgery and role of adjuvant radiotherapy in this setting[53].

TAMIS is a relatively new procedure and as expected several complications have been described. They are all of limited morbidity and occurring in an average of 7.5% of patients[54]. Intra-operative complications include bleeding and entry into the peritoneal cavity, especially for anterior placed and higher lesions. Entry into the peritoneal cavity occurs in about 1% of cases and usually the rectum is closed immediately once the specimen is removed. In these patients it is recommended that gastrografin enema is done on day-3 postoperatively to document the absence of leaks before discharge. Antibiotics may have to be extended if there was significant gross peritoneal contamination. Hemorrhoidal thrombosis, bleeding, pneumoperitoneum, subcutaneous emphysema, urinary retention and urinary tract infections have all been reported immediately post-operatively[45,55]. Later complications include rectal stenosis and rectovaginal fistula[45]. Incontinence, if it occurs is rare and usually self-limiting. Albeit that grossly 100% of specimens have negative margins, there is a 4.1% and 4.4% incidence of microscopic positive margins and tissue fragmentation respectively[54].

Clinical and endoscopic appraisal of the rectum for marginal recurrence should be done at 3, 6, 9 and 12 mo after surgery, and repeated 6-monthly for the next 2 years. Radiological evaluation by MRI for nodal recurrence should be done at 6 mo. Other aspects of the follow-up can be guided by specific criteria such as the NCCN guidelines.

Although there has been significant growth in the use of TAMIS, the majority of reports are for benign disease, specifically villous and tubulovillous adenomas in the lower and mid rectum. Currently the majority of studies report short-term results with limited follow-up and these are case series and small prospective comparative studies. Listed in Table 2 are publications involving more than 15 patients diagnosed with early adenocarcinoma and subjected to TAMIS. These results revealed that the majority of patients have a successful operation, with operative time of about 80 min, length of stay in hospital is one day, positive resection margins is less that 10% and less than 10% of patients have complications[56-59]. The few studies looking at quality of life and functional outcomes reveal that overall quality of life was improved or not impaired after TAMIS, probably due to the removal of the tumor, and at 6 mo was equal to the general population[56,60]. TAMIS can be used after neoadjuvant chemoradiotherapy[61,62] but care should be taken because of the high incidence of wound complications in this setting[46]. We anticipate an increase in the use of TAMIS in these patients given the accumulating evidence that patients with excellent response after neoadjuvant therapy can be managed more conservatively without compromising their survival[63]. The more important role of TAMIS however was as a launching pad for TaTME.

MINIMALLY INVASIVE SURGERY

On the background of the explosion of laparoscopic surgery for colon cancer, there has been similar enthusiasm for its application to rectal cancer where the laparoscopic approach was performed from a standard transabdominal "top down" approach. However, numerous technical difficulties related to operating in the pelvis have often led to longer operative times, a steep learning curve and high conversion rates. In addition, poor ergonomics in the use of an endoscopic linear stapler to divide the distal rectum, often resulted in multiple firings and the concurrent risk of anastomotic leaks[64]. Anastomotic leaks are always to be minimized as mortality from septic complications, increased local recurrence rates in addition to decreased survival have all been well established. Furthermore, albeit with exceptions[14,64] laparoscopic proctectomy has demonstrated increased circumferential margin positivity and concerns of the long-term oncologic outcomes[65,66]. These problems were thought to be resolved with the introduction of the robot to aid with proctectomy[67] but the increased cost prevented its widespread adoption[68]. There maybe some advantage to the use of the robot with a reduction in urinary and sexual dysfunctions after proctectomy, but this remains to be proven with randomized prospective studies[69]. The results of the Robotic *vs* Laparoscopic Approach for the Resection of Rectal cancer (ROLARR) trial are highly anticipated in an attempt to demonstrate any statistical significant advantage conferred by the robotic approach with respect to long-term oncologic outcomes[67]. At the moment robotic-assisted

Table 2 Publications of transanal minimal invasive surgery for early rectal cancer including minimum 15 patients with invasive adenocarcinoma in their study (2010-2016)

Ref.	No. of patients (# with cancer)	Distant from AV	Duration of surgery (min)	Length of stay (d)	Complications (%)	Positive margin: Local recurrence (%)
Albert *et al*[47]	50 (23)	8.1 cm	? NA	0.6	6	6:4
McLemore *et al*[57]	32 (16)	NA	123	2.5	15	NA
Hahnloser *et al*[51]	75 (38)	6.4	77	3.4	19	NA
Gill *et al*[58]	32 (21)	7.5	131	1.1	6	NA
Rega *et al*[59]	55 (26)	NA	78	NA	4	?9
Keller *et al*[49]	75 (17)	10	76	1	4	7:1
Quaresima *et al*[55]	31 (17)	NA	NA	3	9.6	3 (3)

NA: Not reported.

proctectomy for cancer is better confined to educational programs in high volume hospitals in order to avoid an increase in cost and complication rates[68]. Still there are the short-term benefits of reduced analgesic requirements, shortened length of stay in hospital, less wound related complication such that the laparoscopic approach is being widely utilized and to the advantage of the patients[70-72]. Concerns remain despite more recent studies[16,73], and high quality evidence in favor of a standard laparoscopic approach for its routine application to rectal cancer are still elusive. It is in this setting that trans-anal TME "down-to-up approach" was introduced[74,75]. Transanal TME is purported to confer distinct advantages of greater visibility, and a more complete mesorectal excision for mid and low rectal cancer patients, natural orifice specimen extraction with less post-operative pain and fewer wound complications. It was developed to improve the oncologic and functional outcomes of patients with mid and low rectal cancers[76,77]. Other advantages include being able to clearly demarcate the distal resection margin and more options for anastomosis (intersphincteric resection, stapled or hand sewn anastomosis). That the TME (the most important part of the operation) is being performed at an earlier phase in the procedure may also be advantageous with respect to surgeon fatigue.

TaTME occurs when at least the lower third of the rectum is mobilized and resected transanally according to TME principles. It is said to take all the major surgical developments of the last three decades in CRC care (TME, laparoscopy, NOTES) and roll them into one procedure[77]. It is purported to be particularly helpful in patients with a narrow pelvis or significant visceral obesity in whom laparoscopic pelvic dissection is challenging[48]. Still the procedure has a steep learning curve and familiarity with laparoscopic TME and transanal approach to lesions are important pre-requisites. Previously rare complications such as urethral injuries have emerged as the most common major complication of this procedure[78]. Fortunately with proper training and understanding of the anatomy this can be avoided. Experts have also recommended an initial experience preferably with benign disease, female patients and without prior pelvic irradiation[79].

Since its introduction in 2010 there has been several publications on TaTME and the majority of short-term results have demonstrated equivalence or superiority when compared to standard open or laparoscopic surgery[78,80-83]. This is also supported by meta-analyses done by Xu *et al*[84] and Ma *et al*[85] reinforced in the recent systematic review by Arunachalam *et al*[86] showing lower risk of a positive CRM and better quality TME with shorter operative times, and reproducible in patients undergoing neoadjuvant chemoradiation[87]. To date the largest single series is of 140 patients[64] and although the results were of limited follow-up and did not include an evaluation of functional outcome, there were no conversions, operative complications were comparable to the "top-down" laparoscopic and 97% of the resected specimens macroscopically had complete TME. Still there must be a word of caution as the results of the international registry of the first 720 procedures from 66 registered units in 23 countries were recently published showing that conversion occurred in 9.1%, intact TME specimens was achieved in 85% and postoperative mortality and morbidity occurred in 0.5% and 32.6% respectively[88].

TaTME has its detractors[89,90], the operative technique is not standardized, and involves dissecting from within the rectum outwards into the mesorectum with the theoretical risk of contaminating this space and the peritoneal cavity with bacteria[91] or worse malignant cells[90], even when there is routine performance of iodine-based distal rectal washout. While the two-team approach offers efficiency in execution, the procedure calls for just that, two teams, or at least two sets of instruments for the transanal and transabdominal approaches. This again is at least associated with a theoretical risk of increased cost, even if it is reduced by shorter operative times. The already mentioned urethral injury is one possible complication, but anastomotic leaks, bowel injuries, urinary dysfunctions and bleeding have all been described[92]. All these occur in a setting where 98% of cases were diverted proximally with a stoma[70].

There is a concern as to whether TaTME may worsen low anterior resection syndrome but there is a dearth of studies about functional outcome and the quality of life impact of this approach[92]. Studies of long-term superiority (or at least non-inferiority) compared to the usual "top-down" laparoscopic approach are sparse and for now we

await the results of multicenter randomized prospective trials like the COLOR 3 trial[76] and the long-term results of the various registries before this method of rectal cancer resection can be universally recommended.

CONCLUSION

Global trends suggest that the prevalence of rectal cancer will continue to increase in the next few decades with marked geographic variations in the stage of diagnosis and treatment options available. As such the surgical community must strive to continue to provide quality care as dictated by high cure rates and minimal impact on their quality of life for this disease. Watchful waiting after complete pathologic response to neoadjuvant chemoradiotherapy, TAMIS and TaTME all are exciting new options for the management of selected patients with rectal cancer. They add to the gold standard that remains open TME with neoadjuvant chemoradiotherapy or adjuvant chemotherapy where indicated. These newer options all have in common limited evidence in support of their universal adoption and a limited number of skilled surgeons who are experienced in their efficient execution. For now, whilst the evidence accumulates, their widespread introduction should be well controlled and regulated in an environment of well trained practitioners, thus allowing the informed patient to benefit from the advantages these options promise.

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ORIGINAL ARTICLE

Case Control Study

Utility of routine blood tests after elective laparoscopic cholecystectomy for symptomatic gallstones

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Abstract

AIM

To evaluate the value of blood testing after elective laparoscopic cholecystectomy and its association with procedure related complications.

METHODS

Charts of all patients undergoing elective laparoscopic cholecystectomy from January 2013 through December 2014 were reviewed retrospectively for demographics, indication for surgery, operative course and outcome. In our institution the decision to perform postoperative blood analysis is left for the discretion of the surgeon, therefore we had the possibility to compare the results of those who had blood analyses results to those who did not. Analysis was performed to identify variables associated with the decision to perform postoperative blood tests. Subsequently a univariate and multivariate analyses was performed comparing the two cohorts. Secondary subgroup analysis was performed to identify factors associated with procedure related complications.

RESULTS

Five hundred and thirty-two elective laparoscopic cholecystectomies for symptomatic gallstones were performed during the study period. Sixty-four percent of the patients (n = 340) had blood tests taken post operatively. Patients that had laboratory tests taken were older (P = 0.006, OR = 1.01), had longer surgery (P < 0.001, OR = 3.22) had more drains placed (P < 0.001, OR = 3.2) and stayed longer in the hospital (P < 0.001, OR = 1.2). A subgroup analysis of the patients who experienced complications revealed longer stay in the hospital (P < 0.001), higher body mass index (BMI) (P = 0.04, OR = 1.08),

increased rates of drain placement (P = 0.006, OR = 3.1) and higher conversion rates (P = 0.01, OR = 14.6). Postoperative blood tests withdrawals were not associated with complications (P = 0.44). On Multivariate analysis BMI and drain placement were independently associated with complications.

CONCLUSION

The current study indicate that routine postoperative blood tests after elective laparoscopic cholecystectomy for symptomatic gallstones does not predict complications and may have an added benefit in diagnosis and management of cases were the surgeon encountered true technical difficulty during surgery.

Key words: Cholecystectomy; Blood tests; Laparoscopy; Complications; Post-operative; Gallstones; symptomatic

Core tip: Laparoscopic cholecystectomy is the procedure of choice for patients with symptomatic gallstones. Although some patients will need overnight observation many of the younger patients, with low body mass index (BMI), that did not have severe gallbladder infection may be performed under day surgery, in institutions that have the necessary setup. The current study show that postoperative blood analyses does not predict nor correlate with postoperative complications and has no impact on outcome. The only independent predictors of complications on multivariate analysis are BMI and drain placement that was used a surrogate for technical difficulty during surgery. Intuitively length of surgery is thought to be in correlation with technical difficulty. In centers were supervised residents perform high percentage of the operations, length of surgery does not correlate with difficulty or post operative complications and by itself does not seem to indicate need for post-operative blood analyses.

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INTRODUCTION

Cholelithiasis is a common disease affecting millions of people around the world. Laparoscopic cholecystectomy (LC) is the procedure of choice for symptomatic gallstones and more than 500000 procedures are performed annually worldwide. The need for blood tests evaluation after LC is seldom discussed in the literature[1,2]. In our institution postoperative follow-up blood testing is left for the discretion of the attending surgeon in charge of the case. Departmental protocols exist for the treatment of procedural related complications. Post LC liver function tests have been previously shown to be slightly and transiently elevated with no clinical significance[3-6]. We sought to evaluate whether routine blood tests after elective laparoscopic cholecystectomy have any impact on patient's outcome and whether they are predictive of postoperative complications.

MATERIALS AND METHODS

Charts of all patients undergoing elective laparoscopic cholecystectomy from January 2013 through December 2014 were reviewed retrospectively for demographics, indication for surgery, operative course and operative outcome. Post-operative laboratory analyses order during the time frame of the study were left for the discretion of the attending surgeon in charge of the case. Data was compared between the two groups (lab *vs* no lab) to identify factors associated with the surgeon threshold to order blood work postoperatively. A second subgroup analysis was performed to evaluate the differences between patients who experienced complications and patients who did not. Variables that were significant by univariate analysis were subjected to a multivariate logistic regression model to evaluate variables that are independently associated with complications. Primary measure of outcome was surgical complications and secondary measure of outcome was the association of postoperative blood tests with factors such as age, body mass index (BMI), length of surgery and the positioning of a drain.

Statistical analysis

Potential associations were assessed by Fisher's exact test for percentages, *t*-test for means, and Mann-Whitney *U* tests for medians. A series multivariable logistic regressions were applied to identify independent characteristics with a $P < 0.10$ from univariate analysis; these were treated as candidate variables in the models[7]. Factors included in the final regression models were assessed for significance by the likelihood ratio test (LRT). Two-tailed P value < 0.05 was considered statistically significant. Statistical analysis was performed with JMP version 12.1.0 (64 bit), SAS institute inc.

RESULTS

During the study period 532 elective LC for symptomatic gallstones were performed. Mean age of the patients was 48 years; the majority of the patients (73%) were females. Most patients were overweight (71.7%, n = 302) with a mean BMI of 28.6 (Table 1). Two patients (0.4%) were operated for gallstone and had incidental finding of adenocarcinoma of the gallbladder. Both were confined to the mucosa (T1) and were submitted for follow-up alone. Five patients (0.9%) required conversion to open approach. Sixty four percent of the patients (n =

Table 1 General data and demographics *n* (%)

	n = 532
Age (yr)	48.9 ± 17.3
Gender (female)	386 (72.56)
LOS (d) (median)	1.5 (1-7)
Time of Surgery (min) (median)	50 (14-178)
Drain	134 (25.2)
Laboratory analysis	340 (63.9)
BMI (kg/m^2)	28.6 ± 5.6
> 25.1	302 (71.73)
> 30.1	138 (32.8)
> 35.1	52 (12.35)

LOS: Length of stay; BMI: Body mass index.

Table 2 Detailed rate and type of complications *n* (%)

	n = 532
Overall complication rate	21 (3.9)
Biliary damage	5 (0.9)
Hemorrhage	10 (1.9)
Post-operative abscess	5 (0.9)
Urinary tract infection	1 (0.2)

340) had blood tests (complete blood count and routine chemistry including electrolytes, renal and liver function tests) withdrawn post operatively. Overall complications rate was 3.9%. Postoperative bleeding was the most common complication (1.9%, *n* = 10). Three patients were re-operated for this complication. Biliary duct injury and intra-abdominal infection were equally common (0.9%, *n* = 5) (Table 2).

Patients who had post-operative laboratory tests taken were older (*P* = 0.006, OR = 1.01), had longer surgery (*P* < 0.001, OR = 3.22) and stayed longer in the hospital (*P* < 0.001, OR = 1.2) (Table 3). Closed suction drain was placed in 25.2% (*n* = 134) of the patients. Post-operative blood tests were more commonly withdrawn in this subgroup of patients (*P* < 0.001, OR = 3.2) (Table 3).

The primary outcome of the study was complications and the ability of postoperative blood tests to predict them. A subgroup analysis of the patients who experienced complications compared to the ones who did not showed that complications were associated intuitively with longer stay in the hospital (*P* < 0.001), but also with higher BMI (*P* = 0.04, OR = 1.08), higher rate of drain placement (*P* = 0.006, OR = 3.1) and higher conversion rate (*P* = 0.01, OR = 14.6). Interestingly postoperative blood tests were not associated with complications (*P* = 0.44). On Multivariate analysis BMI (0.05) and drain placement (0.02) were both associated independently with complications (Table 4).

To evaluate the differences in pre and postoperative liver function tests we performed the Wilcoxon signed rank test. We found statistically significant increase in aspartate transaminase (AST) and a decrease in alkaline phosphatase (ALP), both with no clinical significance.

Table 3 Comparison of patients with and without laboratory test post operatively *n* (%)

	Laboratory (*n* = 340)	No laboratory (*n* = 192)	*P* value
Age (yr)	50.4 ± 17.7	46.1 ± 16.4	0.006
Gender (female)	239 (70.3)	147 (76.6)	0.12
LOS (d)	1.9 ± 0.99	1.3 ± 0.56	< 0.001
Length of surgery	55 (15-178)	43 (14-100)	< 0.001
BMI (kg/m^2)	28.9 ± 5.8	28.1 ± 5.2	0.17
Complications	18 (3.4)	4 (0.8)	0.07
Conversion	5 (0.3)	0	0.16
Drain	109 (20.5)	25 (4.7)	< 0.001

LOS: Length of stay; BMI: Body mass index.

DISCUSSION

Laparoscopic cholecystectomy is the standard of care for patients with symptomatic gallstones. Preoperative evaluation and its importance are vastly discussed in the literature and are beyond the scope of this article. We sought to focus on the postoperative follow-up of patients and to evaluate the surgeons' threshold to order these tests.

In many institutions LC is performed in day surgery setup. Routine blood testing post-operatively may result in inconvenience to the patient and his family as well as increased overall costs. In the current study we evaluate the surgeons' threshold to order post- operative blood tests. Older age, prolonged surgery and the need for more than one day of hospitalization triggered the need for postoperative blood work. Drain placement is a good surrogate to the complexity encountered by the surgeon during the procedure especially if done electively. In fact patients who had drains placed had significantly more blood test taken. Subgroup analysis to identify factors associated with complications showed that postoperative blood tests were not independently associated with increased rate of complications. In fact the only factors independently associated with increased risk for complications were BMI and drain placement.

Length of surgery was associated with increased risk of complications on bivariate analysis but not on multivariate analysis correcting for BMI, drain placement, length of surgery and postoperative blood withdrawal. Our institution is a university center and residents perform high percentage of the procedures with the supervision of an attending surgeon. Length of surgery may be affected therefore by our teaching duties and not necessarily a true complexity of the cases.

We also evaluated the utility of the blood test taken and whether they have actually changed the management of the patients. In the complication group (*n* = 21), 12 patients were discharged on day one or two. Blood tests were taken to 75% (*n* = 9) of 21 patients in the complication group. All blood work returned normal and the patients were discharged. All these patients were readmitted for complications. This observation

Table 4 Subgroup univariate and multivariate analysis comparing patients who experienced complications with those who did not *n* (%)

	Complications (*n* = 22)	No complications (*n* = 510)	*P* value (univariate)	*P* value (multivariate)
Age (yr)	53 ± 17	48.7 ± 17.4	0.26	
Gender (female)	15 (68.2)	371 (72.8)	0.63	
LOS (d)	2.45 ± 1.2	1.7 ± 0.9	< 0.001	
Length of surgery	57.3 ± 20.7	53.4 ± 23.3	0.44	0.08
BMI (kg/m^2)	31.5 ± 8.1	28.5 ± 5.5	0.04	0.05
Postop labs	18 (81.8)	322 (63.1)	0.07	0.06
Conversion	2 (9.0)	3 (0.6)	0.01	
Drain	11 (50.0)	123 (24.1)	0.006	0.02

LOS: Length of stay; BMI: Body mass index.

suggests that the immediate postoperative blood work did not change the management and did not predict the complications.

In conclusion, the results of our study suggest that routine postoperative blood tests after elective laparoscopic cholecystectomy are unnecessary and should be carried out only in selected cases where the surgeon encountered true technical difficulty during surgery. Length of surgery by itself does not seem to indicate need for blood test postoperatively only when it is accompanied by high level of difficulty. Future prospective studies that address the matter are needed.

COMMENTS

Background

Laparoscopic cholecystectomy (LC) is the procedure of choice for patients with symptomatic gallstones and thousands of these procedures are performed every year worldwide.

Research frontiers

The current study explore the need for routine post operative blood analysis.

Innovations and breakthroughs

Although many places do not take blood samples after uneventful laparoscopic cholecystectomy, gives the evidence for such routine.

Applications

Laparoscopic cholecystectomy may be performed safely under day surgery setup.

Peer-review

This article is an interesting study and suitable for publication in this journal. Authors described utility of routine blood tests after LC.

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ORIGINAL ARTICLE

Observational Study

Value of multi-disciplinary input into laparoscopic management of rectal cancer - An observational study

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Author contributions: Masoud AG and Haray PN conceived and designed of the study; Arif SS, Davies RA, Masoud AG and Haray PN have all contributed to the data; Dhruva Rao PK and Peiris SPM collected, analysed and interpreted the data; all authors have contributed significantly the drafting and revising the manuscript, and approved the version of the article to be published.

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Abstract

AIM

To assess the impact of multi-disciplinary teams (MDTs) management in optimising the outcome for rectal cancers.

METHODS

We undertook a retrospective review of a prospectively maintained database of patients with rectal cancers (defined as tumours $\leqslant$ 15 cm from anal verge) discussed at our MDT between Jan 2008 and Jan 2011. The data was validated against the national database to ensure completeness of dataset. The clinical course and follow-up data was validated using the institution's electronic patient records. The data was analysed in terms of frequencies and percentages. Significance of any differences were analysed using χ^2 test. A Kaplan-Meier analysis was performed for overall survival and disease free survival.

RESULTS

Following appropriate staging, one hundred and thirty-three patients were suitable for potentially curative resections. Seventy two (54%) were upper rectal cancer (URC) - tumour was > 6 cm from the anal verge and 61

(46%) were lower rectal cancers (LRC) - lower extent of the tumour was palpable ⩽ 6 cm. Circumferential resection margin (CRM) appeared threatened on pre-operative MRI in 19/61 (31%) patients with LRC requiring neo-adjuvant therapy (NAT). Of the 133 resections, 118 (89%) were attempted laparoscopically (5% conversion rate). CRM was positive in 9 (6.7%) patients; Median lymph node harvest was 12 (2-37). Major complications occurred in 8 (6%) patients. Median follow-up was 53 mo (0-82). The 90-d mortality was 2 (1.5%). Over the follow-up period, disease related mortality was 11 (8.2%) and overall mortality was 39 (29.3%). Four (3%) patients had local recurrence and 22 (16.5%) patients had distant metastases.

CONCLUSION

Management of rectal cancers can be optimized with multi-disciplinary input to attain acceptable long-term oncological outcomes even when incorporating a laparoscopic approach to rectal cancer resection.

Key words: Rectal cancer; Multi-disciplinary management; Laparoscopic rectal resection outcomes

Core tip: Recently, management of rectal cancer has undergone a process of standardization with introduction of total mesorectal excision and use of neo-adjuvant long course chemo-radiotherapy. In the United Kingdom, multimodal therapy is provided under the auspices of multi-disciplinary teams (MDTs). This is the first study to report on the benefits of managing patients jointly within such an MDT.

Dhruva Rao PK, Peiris SPM, Arif SS, Davies RA, Masoud AG, Haray PN. Value of multi-disciplinary input into laparoscopic management of rectal cancer - An observational study. *World J Gastrointest Surg* 2017; 9(6): 153-160 Available from: URL: http://www.wjgnet.com/1948-9366/full/v9/i6/153.htm DOI: http://dx.doi.org/10.4240/wjgs.v9.i6.153

INTRODUCTION

Rectal cancer accounts for a third of patients with large bowel cancer[1,2]. Historically, management of rectal cancers has been of variable standard with significant differences in local recurrence rates[3-6]. The Association of Coloproctology of Great Britain and Ireland (ACPGBI) and the National Institute for Health and Care Excellence (NICE) have both recommend that rectal cancer should be managed by a multi-disciplinary team (MDT)[7,8]. This has led to initiatives to standardize MDT practises across the country.

Currently, nearly 90% of patients with colorectal cancer undergo discussion and treatment planning at an MDT in the United Kingdom[2]. Total mesorectal excision (TME) has been established as the gold standard for the management of mid and lower rectal cancers over the last few years following the results of numerous trials such as the MR CR07 and Dutch TME trials[5,6,9]. The role of neo-adjuvant therapy is also well established in patients with threatened margins[7,8].

We have had an established MDT team managing colorectal cancer since 1997. Our unit has been performing laparoscopic rectal resection under the auspices of the MDT since 2000, initially in selected cases and since 2008, with increased experience, as the default approach. NICE recommends laparoscopic rectal resection by experienced surgeons[10].

We undertook this retrospective analysis of a prospectively maintained database to assess the effectiveness of our MDT rectal cancer management outcomes.

MATERIALS AND METHODS

Definitions

Rectal cancer = All cancers ⩽ 15 cm from anal verge as measured during rigid sigmoidoscopic examination were classified as rectal cancers. These were further categorized as below: Lower rectal cancer (LRC) = All palpable tumours (⩽ 6 cm from anal verge); upper rectal cancer (URC) = All other tumours (6-15 cm from anal verge); Circumferential resection margin (CRM) positivity = if CRM < 1 mm (Both on pre-op MRI and at histopathology); Local or distant metastasis was defined on the basis of radiological evidence.

MDT

Our MDT consists of 3 colorectal surgeons, 1 specialist GI clinical oncologist, 2 specialist radiologists, 1 pathologist, 1 colorectal specialist nurse, 1 enhanced recovery co-ordinator, 2 enterostomal therapists, 1 palliative care consultant/specialist nurse and 2 gastroenterologists. This team meets every week and has been active since 1997 with a track record of publications, awards and innovative solutions to enhancing quality of care and patient experiences[11-13]. Non clinical business meetings of the team are held to facilitate the formulation and agreement of local protocols for colorectal cancer diagnosis, investigations and treatment.

Staging

All patients diagnosed with rectal cancer were staged with a computerized tomography (CT) scan of thorax, abdomen and pelvis. They also underwent either a colonoscopy or a CT colonogram (done as a part of staging CT). All patients with LRC and some with URC underwent a magnetic resonance imaging (MRI) of rectum for local staging as per the T2 weighted fast spin echo protocol, in 5 mm slices in the axial, coronal and sagittal planes in addition to oblique axials targeted at right angles to the axis of the tumour, using 3 mm slices and smaller "Field of View" for maximal resolution. As per common practice

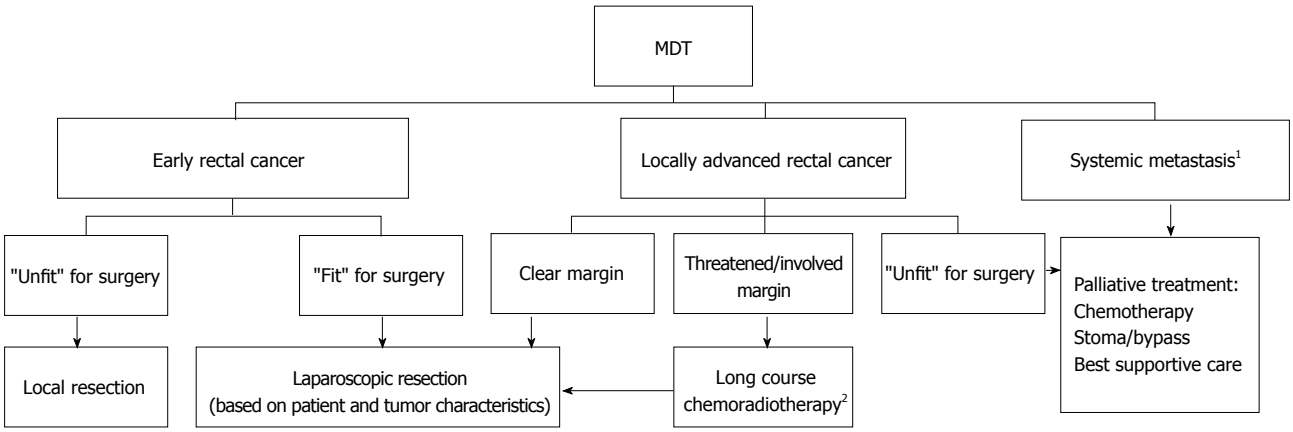

Figure 1 Multi-disciplinary team protocol. [1]If metastases were deemed resectable, referral made to appropriate specialty and primary treated with curative intent. [2]45 Gy in 25 fractions to the pelvis over 5 wk with concurrent capecitabine chemotherapy. MDT: Multi-disciplinary team.

in the United Kingdom, none of our patients underwent endo-rectal ultrasound scanning.

Treatment planning

The staging investigations of all patients were reviewed by the MDT and treatment plans formulated according to the MDT protocol (Figure 1). Patients with threatened CRM were offered neo-adjuvant therapy (NAT) given as a pre-operative Long Course Chemo-Radiotherapy (LCRT), 45 Gy in 25 fractions to the pelvis over 5 wk with concurrent Capecitabine chemotherapy. In addition, short course radiotherapy 25 Gy in 5 fractions over 1 wk was considered in patients with moderate risk rectal cancers. The patients were then restaged and reviewed at MDT prior to surgery. Cases considered suitable for resection were scheduled for surgery 6-10 wk following NAT.

All patients with URC were planned for an anterior resection (AR). Planned surgical options for patients with LRC were either total mesorectal excision with de-functioning ileostomy (TME + I) or when the sphincters or levators were threatened, an abdomino-perineal excision (APER).

Post-operative histology was reviewed by the MDT and clinically fit patients with poor prognostic features on histology were offered adjuvant treatment (AT) with Oxaliplatin and 5 fluorouracil based combination chemo-therapy.

Surgical procedure

The default surgical approach was laparoscopic resection except when the patient had had multiple previous surgery, anaesthetic considerations precluded a laparoscopic approach and occasionally due to technical issues such as particularly obese male patients with bulky tumours not responsive to neo-adjuvant treatment. We defined conversion as previously published[12]: (1) If the final incision made was longer than planned pre-operatively; (2) If the incision needed to be made at an earlier stage of the operation than planned pre-operatively; and (3) If the incision was made at a site other than that planned pre-operatively.

All laparoscopic procedures were performed by one of two consultant surgeons (each with experience of over 100 colorectal resections at the beginning of the study period) or by senior trainees under direct supervision (consultant scrubbed). All procedures were performed with the patient in the Lloyd Davies position with steep Trendelenburg tilt, following a step-wise approach (Table 1)[14,15]. The open procedures and the converted cases followed a similar step-wise approach through a midline laparotomy.

Follow-up protocol

All patients were reviewed initially at 6 wk after their surgery. The follow up protocol was a 6 monthly clinical review with haematological and biochemical tests including tumour marker CEA for 5 years, an annual CT scan of thorax, abdomen and pelvis for 3 years and a surveillance colonoscopy at 3 and 6 years. The length of follow-up was recorded in months from the date of operation.

Patients included in this study

After appropriate institutional approvals, all patients with rectal cancer discussed at our MDT meeting between Jan 2008 and Jan 2011 were identified and the patient demographics, treatment, post-operative histology and follow-up data were studied.

Outcome measures

The primary outcome measures of the study were local recurrence rates and disease free survival. The secondary outcome measures included post-operative length of stay, major complications and overall survival.

Statistical analysis

The data was analysed in terms of frequencies and percentages. Significance of any differences were analysed using χ^2 test. A Kaplan-Meier analysis was performed for overall survival and disease free survival.

RESULTS

During these 3 years, a total of 141 patients [median age 67 years (range 45-89); M:F = 1.7:1] were diagnosed

Table 1 Stepwise approach to rectal dissection

1	Port positions: 10-12 mm - sub-umbilical, RUQ (camera), RIF and LIF; patient in Lloyd-Davies position
2	Omentum to supracolic compartment and small bowel stacking
3	Identify right ureter
4	Start medial dissection at the promontory
5	Identify left ureter, then left gonadal, pelvic nerves
6	Protect left ureter with surgicel® and Pedicle dissection
7	Identify ureter through both windows of mesentery either side of pedicle
8	Transect pedicle, confirm haemostasis
9	Left lateral dissection, identify left ureter and proceed up to peritoneal reflection; IMV high tie and splenic flexure mobilisation, if required
10	Mesorectal Dissection and preparation of rectum for division1
	Right mesorectal dissection up to peritoneal reflection
	Posterior dissection (presacral plane down to levator), keep left ureter in view
	Divide peritoneal reflection anteriorly and dissect till seminal vesicles/vaginal fornix
	Complete both lateral dissection, identify the ureters all the way
	Anterior dissection keeping to the plane just posterior to the vesicles/vagina
	Rectal Cross stapling (achieve antero-posterior staple line) or proceed to perineal dissection[1]
11	Intra-corporeal cross stapling of rectum at appropriate level protecting lateral and anterior structures and Grasp stapled end of specimen
12	Left iliac fossa port extended as a transverse incision for specimen delivery; protect wound and deliver specimen by the stapled end
13	Complete mesenteric ligation, proximal bowel division and prepare proximal bowel for anastomosis
14	Close wound, re-establish pneumoperitoneum
15	Intra-corporeal bowel anastomosis with no tension, no twist and vital structures protected
16	Close incisions

[1]In patients undergoing laparoscopic abdomino-perineal excision, the left sided port is placed at the site of the planned colostomy and the laparoscopic dissection stopped at the mid rectal level, the proximal colon divided intra-corporeally with a stapler and proceed to a wide excision of the anal sphincter complex to obtain a cylindrical specimen.

with rectal cancer. Of these, there were 2 patients with locally advanced disease invading prostate and so were referred for exenteration elsewhere. A further 6 patients went on to have palliative treatment due to either advanced presentation or significant medical co-morbidities. The remaining 133 patients were staged as suitable for potentially curative resections. Of these, 72 (54%) were upper rectal tumours (URC) and 61 (46%) were lower rectal tumours (LRC). Three (2%) patients had resectable metastases at diagnosis and were treated with primary rectal resection, followed by chemotherapy and surgery for metastases.

The pre-operative (putative) CRM was threatened in 19 (14%) patients (4 patients due to presence of nodes close to the CRM). Of these, 14 patients had LCRT; 1 had short course radiotherapy (25 Gy in 5 fractions over 1 wk). Four patients did not receive any Neoadjuvant therapy: 1 female patient with an anterior tumour where there was lack of consensus on preoperative staging being T2 *vs* T4 and 3 patients where there was a small node of doubtful significance threatening the margin.

Interval between completion of NAT and surgery was a median 10 (6-24) wk. One patient had a radiological complete response to neo-adjuvant therapy and opted initially for a watch and wait policy prior to eventually opting to receive surgery.

Table 2 summarizes the operations performed. All 72 patients with URC underwent an AR. Of the 61 with LRC, 29 had TME + I, 1 patient had a TME Hartmann's procedure and 27 had APER. Four patients had TME and anastomosis without covering ileostomy. Surgery following NAT was either APER (8/15) or TME + I (7/15).

Laparoscopic resection was attempted in 118/133 (89%). Conversion rate was 5% (6 out of 118 patients).

Table 2 Operations (n = 133)

Operations	Laparoscopic (conversion)	Open	Total
Anterior resections	66 (2)	6	72
TME	4		4
TME + I	25 (1)	4	29
TME Hartmann's	1 (1)		1
APER	26 (2)	1	27

TME: Total mesorectal excision; APER: Abdomino-perineal excision.

The reasons for conversion were uncontrollable bleeding from the IM pedicle (n = 1), low tumour in a male pelvis, requiring a suprapubic incision rather than the planned left iliac fossa incision for specimen delivery (n = 1) and dense adhesions (n = 4), requiring incisions either larger than planned or at an earlier stage of the operation). The remaining 15 patients (11%) underwent a planned open procedure due to previous extensive surgery, locally advanced tumour in an android pelvis or poor response to LCRT.

Median post-operative length of stay was 5 d (3-49). Major complications needing re-operation within 30 d occurred in 8 (6%) patients [Anastomotic leak: 2, Pelvic haemorrhage requiring packing: 2, Small Bowel Obstruction: 2 (1 - port site; 1 - pelvic), Intra-abdominal collection: 1, Wound dehiscence: 1].

Post-operative histology is shown in Table 3. One hundred and twenty four patients (93.3%) had R0 resection and 9 (6.7%) had an R1 resection (CRM positive - 6 due to tumour, 3 due to nodes). There were no R2 resections in this cohort. Median LN harvest was 12 for the laparoscopic group and 10 for the open group (P < 0.01). Of the 9 patients with positive CRM 4 were URC

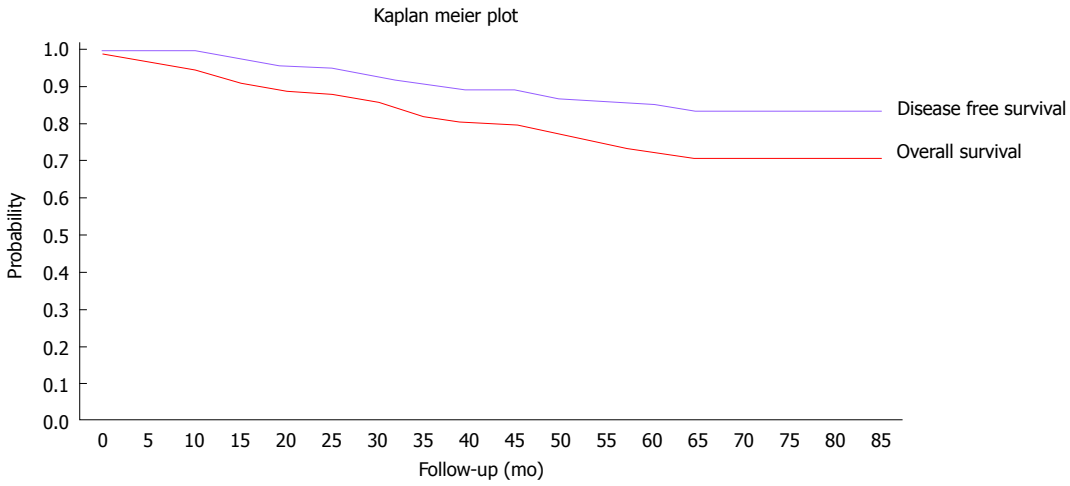

Figure 2 Survival curves for the cohort.

Table 3 Post-op stage (n = 133)

Post-op stage	*n*
R0 resection	124
R1 resection (CRM + ve)	9
R2 resection	0
T1	14
T2	42
T3	58
T4	17
N0	85
N1	31
N2	15

and 5 were LRC. The pre-operative MRI had accurately predicted this in all 5 LRC patients, 4 of whom had received NAT. None of the URCs had had pre-operative MRI as per our practice at that time and so could not be predicted and they did not receive any NAT.

Fifty-six patients had adverse features on histology making them eligible for adjuvant therapy (AT). Of these, 13 were unfit and 3 declined the offer of further chemotherapy. The remaining 40 patients underwent AT.

Median follow up was for 53 mo (0-82). Long-term complications occurred in 9 (6.7%) patients (parastomal hernia: 6, port site hernia: 1, anastomotic stricture: 1, late onset left ureteric obstruction due to fibrosis: 1).

The 90-d mortality was 1.5% (2 patients: 1 in-hospital due to anastomotic leak; 1 patient post discharge - cause unknown). Disease related mortality over the follow-up period was 11 (8.2%); however, overall mortality for the follow-up period was 39 (29.3%).

Four patients (3%) had local recurrence. The durations to development of local recurrence were 15, 23, 33 and 39 mo. On further analysis of the sub-group with local recurrence, only 1 patient had had a histologically positive CRM. This patient had an upper rectal tumour and had not been considered for NAT. The other 3 patients having local recurrence were all T3 URC and all had had a R0 resection with CRM clearance of between 1-2 mm. In this cohort, we had no local recurrence in any patients with LRC.

Twenty two patients (16.5%) developed distant metastases and one patient developed metachronous colonic cancer. Four of these had no poor prognostic factors on histology such as node positive disease, extra-mural lympho-vascular invasion and/or poor differentiation. Of the 18 with poor prognostic markers, 3 had declined and 5 had been deemed unfit for AT. Figure 2 shows the Kaplan-Meier curve for our cohort.

DISCUSSION

Patients in our unit have been receiving care under the MDT umbrella since 1997. Our unit has a relatively high uptake of laparoscopic rectal resections with 89% undergoing laparoscopic resection with a relatively low conversion rate using strict definitions for conversion. The median length of stay was 5 d and is comparable to most enhanced recovery programmes. Oncological results too are acceptable with a CRM positivity rate of 4% for sphincter saving resections (4 out of 106 patients) and 18% for APER (5 out of 27 patients). LNH was higher following laparoscopic resection, in keeping with other studies[16].

MDT management is a concept propagated by practice with no "research/trial" based evidence. There is no level 1 evidence that supports MDT, no grade of recommendation is provided for its use in national guidelines and yet, this concept is gaining acceptance worldwide. MDT management has been a mandatory requirement for treatment of cancers in United Kingdom since 2000. For this reason, we cannot perform a meaningful comparative analysis of patients who have not received care under the MDT umbrella. The management of the rectal cancer has also undergone a significant change over this period. This precludes use of a historical cohort for comparison as there could be other confounding factors that influence outcomes.

We believe that this the first observational study attempting to clarify the role of various MDT members who make individual specialist contributions, based on

Table 4 Comparison of circumferential resection margin positive

Type of operation	Dutch TME trial[6]	CLASICC trial[5]	MR CRO7 trial[9]	Our series
Sphincter saving resection	13%	10%	8%	3% (4/106)
APER	29%	21%	17%	18% (5/27)

TME: Total mesorectal excision; APER: Abdomino-perineal excision.

consensual decisions arrived at by a group of experts, resulting in improved clinical effectiveness.

Lap TME has been shown to be safe with acceptable short-term clinical and oncological outcomes[5,17-19]. The 2 most recent trials, ALaCaRT and the ACOSOG Z6051, have not been able to demonstrate the non-inferiority of laparoscopic resections compared to open resections in terms "completeness of excision" using a composite scoring system[20,21]. However, they are still accruing data on long term oncological outcomes. Laparoscopic TME can be technically challenging and should be undertaken by experienced surgeons[12,20-22]. Caution should therefore be exercised when evaluating results of laparoscopic TME when the expertise of the surgeons has not been defined. The senior surgeons have had a mean experience of 6 years between them with over 100 laparoscopic resections each prior to the commencement of this study. From this study, we see that acceptable long-term oncological results can be safely achieved when laparoscopic approach is pragmatically applied by appropriately trained surgeons in the context of multimodal therapy overseen by MDT.

The few RCTs reporting 5 year survival were not specifically designed or powered for long term outcomes[3]. More recently several meta-analyses published have not come up with any strong conclusions either way with respect to long-term survival[3,4,19,23,24]. However, laparoscopic resection seems to be associated with a lower local recurrence rate[24]. This lack of clarity has been the cause for variable uptake of Lap TME ranging from 0%-100%[2,25].

We believe that this study is one of the first to report on outcomes of laparoscopic rectal resections outside of RCTs or case control studies. Tables 4 and 5 show our results which compare favourably to other published studies. Figure 2 shows the Kaplan Meier curves for our cohort which shows an overall survival of 81% and disease free survival of 90% at median follow-up. This compares favourably with other series with similar follow-up which have reported a predicted overall survival of 81% and disease free survival of 70%[26]. Our survival figures show that our cohort of patients were more likely to die from other causes than from disease recurrence, in keeping with the high co-morbidity of our catchment population[27], most of which falls within the highest quintile of the deprivation index in the United Kingdom.

A 12-year follow-up of Dutch TME trial cohort showed local recurrence of 6.5% (68 patients) in 1082 patients who had an R0 resection[28]. In comparison, we observed a local recurrence rate of 2.4% (3 patients) in 124 patients having an R0 resection. All recurrences were in patients with URC with no recurrences in LRC. We observed only 1 local recurrence in 9 patients who had an R1 resection (11.1%). However extrapolating similar data from the Dutch TME trial would give a figure of 20.8% patients with involved margins developing a local recurrence. This comparison however, may be misleading as the follow up in our study (53 mo) is shorter than the Dutch TME trial (12 years).

Traditionally, local recurrence after rectal cancer resection usually presents within 2 years[2,28]. In our series, we have had a median follow up of 53 mo and have not noticed any local recurrence in the LRC group. The follow-up of the Dutch TME trial cohort confirmed that pre-operative radiotherapy not only reduced local recurrence but was especially effective in preventing anastomotic recurrences[28]. The same effect probably accounts for the absence of local recurrence noted in our study for the low rectal cancers in spite of 10% (6 of 61 LRC) CRM positivity. Another hypothesis worth considering could be that CRM positivity due to lymph nodes may carry a lesser risk of local recurrence when compared with cases where the CRM was involved by the primary tumour.

We believe this observed low rate of local recurrence is due to effective working within a well-established specialist MDT, resulting in appropriate use of NAT for our cohort of patients.

In conclusion, this study demonstrates that good long term oncological outcomes can be achieved for patients with rectal cancer when appropriate multi-disciplinary expertise is combined with surgery being performed by adequately trained surgeons. Neo-adjuvant chemo-radiotherapy improves the oncological outcomes without precluding the routine use of the laparoscopic approach to rectal resection.

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The authors would like to thank all members of the MDT for their commitment to providing high quality care to these patients. In particular, we would like to acknowledge Mr Shah PR (surgeon), Mrs Lewis M, Mrs Williams D, Mrs Howells S (specialist nurses) for their contribution to maintaining the database and Mr Brown C (trainee) for help in updating the follow-up data.

COMMENTS

Background

Rectal cancer accounts for a third of patients with large bowel cancer. Historically, management of rectal cancers has been of variable standard with significant differences in local recurrence rates. The Association of Coloproctology of Great Britain and Ireland (ACPGBI) and the National Institute for Health and Care Excellence (NICE) have both recommend that rectal cancer should be managed by a multi-disciplinary team (MDT). This has led to initiatives to standardize MDT practises across the country. The authors undertook this retrospective analysis of a prospectively maintained database to assess the effectiveness of the MDT rectal cancer management outcomes.

Table 5 Comparison of local recurrence

	Meta-analysis[4] (*n* = 1544)	Dutch TME trial[6] (*n* = 1586)	CLASICC trial[5] (*n* = 400)	MRC CR07 trial[9] (*n* = 1350)	Our series (*n* = 133)
Local recurrence	13%	8%	6.80%	7%	3% (4/133)

TME: Total mesorectal excision.

Innovations and breakthroughs

Providing evidence to the concept of multidisciplinary management of rectal cancer; optimizing outcomes following laparoscopic rectal resection.

Applications

This study adds evidence to the increasing evidence in the evolving management of rectal cancers

Terminology

MDT consists of Colorectal Surgeons, Specialist GI Clinical Oncologist, Specialist GI Radiologists, Specialist GI pathologist, Colorectal Specialist Nurse, Enhanced Recovery co-ordinator, Enterostomal Therapists, Palliative care specialists and Gastroenterologists.

Peer-review

This is a good paper, showing that excellent results can be achieved by dedicate teams. This retrospective analysis focus on the MDT (several related specialities coming together every week) on rectal cancer management and they suggest MDT for better early and late outcomes and for laparoscopy.

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