**Name of Journal: *World Journal of Gastrointestinal Surgery***

**ESPS Manuscript NO: 32399**

**Manuscript Type: Review**

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

Plummer JM *et al.* Advances in rectal cancer

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**Author contributions:** Plummer JM, Leake PA and Albert MR contributed equally to the writing of this manuscript.

**Conflict-of-interest statement:** Plummer JM and Leake PA have no relevant disclosures. Albert MR’s disclosures are: Applied Medical - Consultant; ConMed - Consultant and Surgiquest - Consultant.

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**Manuscript source:** Invited manuscript

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**Received:** January 6, 2017

**Peer-review started:** January 10, 2017

**First decision:** February 17, 2017

**Revised:** March 19, 2017

**Accepted:** April 6, 2017

**Article in press:**

**Published online:**

**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, and 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

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**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 treating 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; In press

**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[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 cannot 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 rectal cancer must be informed of all their 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 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 techinques, 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 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 neoadjunant 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[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[34] concluded radiological evaluation by ERUS, MRI and CT, while done, 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[34]. 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 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.

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 versus 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[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[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 gastrograffin 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 months. 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, LOS 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 months 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 versus 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 approachwith respect to long-term oncologic outcomes[67]. At the moment robotic-assisted 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[84] and Ma[85] reinforced in the recent systematic review by Arunachalam[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 be strive to and 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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**P-Reviewer:** Ammendola M, Facciorusso A, Guerra F, Kaya B, Klinge U, Ulrich A **S-Editor:** Ji FF **L-Editor: E-Editor:**

**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[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.

**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) | 8.1cm | ? NA | 0.6 | 6 | 6:4 |
| McLemore *et al*[57] | 32 (16) | NA | 123 | 2.5 | 15 | NA |
| Hahnloser[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)  | N/A  |  N/A  | 3  |  9.6  | 3 (3%) |

NA: Not reported.