

## **UC Irvine**

### **UC Irvine Previously Published Works**

#### **Title**

Minimally invasive surgery for rectal cancer.

#### **Permalink**

<https://escholarship.org/uc/item/3nw4v1rn>

#### **Journal**

Minerva Surgery, 71(5)

#### **ISSN**

2724-5691

#### **Authors**

Fazl Alizadeh, Reza  
Stamos, Michael J

#### **Publication Date**

2016-10-01

Peer reviewed

# Minimally Invasive Surgery for Rectal Cancer

Reza FAZL ALIZADEH, Michael J. STAMOS \*

Division of Colon and Rectal Surgery, Department of Surgery, University of California, Irvine School of Medicine, CA, USA

\*Corresponding author: Michael J. Stamos, Department of Surgery, University of California, Irvine School of Medicine, 333 City Blvd. West, Suite 1600, Orange, CA92868, USA. E-mail: [mstamos@uci.edu](mailto:mstamos@uci.edu)

## ABSTRACT

Minimally invasive surgical treatments for colon cancers have revolutionized surgical approaches and have been implemented broadly over the last two decades. On the other hand, robotic-assisted *versus* laparoscopic resections for rectal cancer and comparison of these minimally invasive approaches with the traditional open operation are controversial and challenging topics to discuss between the different surgical investigators. Recent published studies have shown somewhat differing data and results from randomized controlled and non-randomized trials comparing laparoscopic with open rectal resections as well as robotic-assisted with both open and laparoscopic approaches. The surgical approach for rectal cancer is a fascinating subject since there are several different endpoints which have been used to measure quality and outcome. Overall survival, disease free survival, and quality of life (QOL) are the most relevant endpoints of rectal cancer treatment. Among minimally invasive approaches, the robotic approach seems to be less invasive than conventional laparoscopic surgery (LS) and less than hand assisted approach due partly to the less traumatic intra-abdominal handling of tissues. A convincing clinical benefit of minimally invasive rectal cancer approaches could be due to diminished surgical stress response leading to reduced morbidity. For this review, we have performed a systematic review of rectal cancer surgical management focusing on minimally invasive approaches, focusing specifically on the latest results of randomized trials for robotic assisted and laparoscopic rectal cancer resection.

**Key words:** Minimally invasive surgical procedures - Rectal neoplasms - Robotic surgical procedures.

Colorectal cancer is the third most commonly diagnosed malignancy worldwide and the fourth most common cause of death 1 and rectal cancer by itself accounts for nearly 40,000 newly diagnosed cases per year in the United States.<sup>2</sup> Rectal cancer management still remains as a complex subject and often mandates a multidisciplinary approach based on a thorough evaluation of tumor location, staging, and resectability. Multimodality treatment and the optimization of surgical approach have led to improved prognosis for locally advanced rectal cancer with local recurrences decreasing from 40% to less than 10% and overall survival increasing from 50% to 75% in the last few decades.<sup>3</sup> Surgical resection has been broadly accepted as the core and primary curative treatment for rectal cancer (stage I, II or III).<sup>4</sup> A comprehensive patient evaluation, in addition to appropriate imaging, are the most important factors that allow a selection of the proper surgical approach and other subsequent therapeutic decisions.<sup>5</sup>

The development of minimally invasive procedures over the last few decades has changed the entire perspectives of the treatment strategies in most surgical specialties. In terms of colon and rectal surgery, minimally invasive operations have been broadly performed for colorectal disease including cancer. Recently, the trend of minimally invasive approaches for colorectal cancer is increasing, to the point that laparoscopic colectomy procedures have been adopted and accounts for the majority of the colectomy resections performed laparoscopically in the United States,<sup>6</sup> but adoption of minimally invasive approaches for rectal cancer is moving forward much slower. In addition to laparoscopic approaches, which have remained as a controversial topic in terms of outcomes compared with open surgery, robotic-assisted rectal surgery has also surfaced as an alternative. Robotic procedures are purported to provide superior visualization within a narrow pelvic field and more precise dissection <sup>7</sup> to achieve a better surgical performance. Ongoing randomized studies will provide additional insight into the role of laparoscopic and minimally invasive robotic surgery for rectal cancer. We

have reviewed the commonly performed methods of rectal cancer surgery focusing on minimally invasive approaches and will discuss results of the latest trials, and conjecture on future perspectives.

## **Background of rectal cancer surgical approaches**

The first successful radical surgical treatment of rectal cancer was reported by Miles in 1908.<sup>8</sup> This was a major breakthrough, and since then development has progressed immensely. However, there has been ongoing controversy over the past century regarding the ideal procedure for the treatment of cancer with the lowest rates of postsurgical complications, recurrence, and mortality. Generally speaking, rectal cancer procedures are either local resections (*i.e.*, transanal) or via an abdominal approach.

### *Local resections*

In terms of surgical classification, there are four methods for local resection including transcoccygeal, transsphincteric, transanal, and transanal endoscopic microsurgery (TEM); the first two approaches have been essentially discarded due to higher incidence of complications and poor overall survival.<sup>9</sup> The selection criteria for performing a local excision are described as patients with cancers limited to submucosa, negative imaging of metastatic disease to regional nodes (N0), tumors less than 3 cm in diameter, located in middle to distal rectum, low risk of developing positive regional lymph nodes (*e.g.* no adverse histologic features), and compliance with aggressive postoperative surveillance.<sup>5, 10-12</sup>

TEM was developed by Buess and Raestrup in 1983,<sup>13</sup> which is a minimally invasive technique for endoluminal resection of local tumors, located 4 to 18 cm above the anal verge and can be performed even without using general anesthetic. It can successfully treat those tumors which are not removable by colonoscopic procedures and can spare some patients the risks and side effects of major rectal surgery.<sup>14</sup>

### *Transabdominal resections*

Transabdominal operations, which can be performed open or minimally invasive, are categorized as sphincter ablating (abdominoperineal resection [APR]) and sphincter-sparing approaches. The first APR procedure done by Miles, was described as resection of the rectum, sigmoid, mesorectum, nodes of the iliac bifurcation, and a perineal component to include the anus and levator ani muscles. Miles reported a high postoperative mortality rate for the procedure, but importantly there was a significant decrease in local recurrence rate.<sup>15</sup> Following his report, APR became the gold standard procedure for all rectal cancers for a few decades and several different surgical investigators made numerous modifications in terms of patient positioning, preoperative care, wound management, colostomy creation, use of drains, and adjuvant therapy.<sup>16</sup> The frequency of APR procedures started to decrease in the 1980's and 90's<sup>17</sup> as a result of several factors such as a more detailed comprehension of the importance of distal margins (the deep, lateral, and radical margins are the decisive factors for recurrence and adequacy of resection),<sup>18</sup> surgical technique innovations, the development and adoption of the circular stapler and double staple techniques, defining of reconstruction methods, advancements in multimodality preoperative chemoradiation therapy as an adjunct to surgical methods, and finally, a recognition of the importance of proper surgical technique.<sup>19</sup>

Sphincter-sparing procedures include low anterior resection (LAR) with colorectal anastomosis, ultra-LAR with coloanal anastomosis, transabdominal transanal resection (TATA) including intersphincteric resection (ISR), and total proctocolectomy with ileal J-pouch anastomosis. The main goal of these procedures is preservation of the anorectal sphincter function to provide a better quality of life for the patients.

Appropriate understanding of the importance of rectal resection margins and anatomical landmarks in rectal cancer operations is essential to choosing the best surgical approach. Since achieving a negative margin is the ultimate objective of determining an adequate rectal resection, development of surgical methods to ensure a negative resection margin would decrease the recurrence rates in patients and provide a better quality of life.

Rectal resection margins are divided into three groups: proximal, distal, and radial (AKA circumferential resection margin [CRM]). In the mid-twentieth century, Claude F. Dixon from Mayo clinic, reported a successful trial of anterior resection approach for cancers of the middle and upper rectum. He proposed the anterior resection as the ideal procedure for the tumors are located in upper half of the rectum and that an APR is the preferred procedure for cancers below this level. He proposed a 5 cm negative proximal and distal margin as the ideal minimal length.<sup>20</sup> Currently, the acceptable optimal negative distal margin is 2 cm length for most resections performed in combination with a total mesorectal excision (TME).<sup>5, 21, 22</sup> However, a 1 cm distal negative margin (or even less) is actually satisfactory for cancers located at or below the mesorectal margin.

Proximal margins are still stated as ideally being 5 cm or greater but the actual importance of this length has never been well defined or studied. Typically, the proximal margin is determined by the residual colon blood supply after the appropriate oncologic (lymphatic) resection rather than a concern for intramural tumor spread.<sup>21</sup> Radial (CRM) margin has become recognized as being far more important in terms of prognostic in rectal cancer, because the involvement of this margin has been correlated with higher rates of local recurrence and a poor prognosis.<sup>23, 24</sup>

#### *TME*

TME is the technique to dissect the perirectal areolar tissue plane (the “holy plane”) including the lateral and circumferential margins of the mesorectal envelope. It was introduced as a concept by Heald in 1982,<sup>25</sup> and since then this method has led to local recurrence rate reduction and oncologic outcomes improvement due to widespread dissemination and adoption.

TME method has reformed the conventional blunt approach commonly used previously for APR or low anterior resection. With TME, the surgeon resects 3 to 5 cm of mesorectum beyond the primary tumor.<sup>21</sup> Anatomically, the rectum and mesorectum are attached to the pelvic floor by a “tube” of anorectal muscle, and the mesorectum ends 1 or 2 cm above the anorectal angle.<sup>19</sup> During an optimal TME, the rectal mesentery (mesorectum) is removed sharply under direct visualization ensuring autonomic nerve preservation, excellent hemostasis, and avoidance of violation of the mesorectal envelope.<sup>26</sup> The mesorectum, including the lateral and circumferential margins of the mesorectal envelope is typically resected to a level 5 cm below the lower margin of the tumor, but not necessarily to the level of the pelvic floor.<sup>5</sup> During the last two decades, TME has become the standard surgical approach to mid and low rectal cancer resection and it also has improved local control of rectal cancer through a dissection that removes the disease-bearing lymphatic tissue around the rectum and maintains fascial containment of the primary tumor.<sup>27</sup> The local recurrence rate following inclusion of a TME with an APR or sphincter-sparing procedure has been reported from 4 to 7 percent.<sup>24, 28-31</sup>

### **Minimally invasive approaches for rectal cancer**

Minimally invasive procedures utilize innovative technologies to avoid the need for the large incisions used in traditional open surgery. The development of these techniques has been an important advance for the benefit of patients and is utilized for the treatment of various surgical disorders. It is fundamental to accept that the minimally invasive treatment of rectal cancer should follow the same surgical oncologic principles as the open procedure. Minimally invasive surgery was introduced in 1987 with the first laparoscopic cholecystectomy.<sup>32</sup> Since then, laparoscopic procedures have been advanced and developed by improvements in technology and augmented technical skill of surgeons. Recently, randomized controlled data have demonstrated surgical and oncologic outcomes of laparoscopic colon surgery similar to those for open surgery. However, the technical challenges of performing laparoscopic resection of rectal cancers and the uncertainty of the oncologic quality of the surgical resection have prevented the ideal growth of minimally invasive rectal surgery.<sup>7</sup>

#### *Laparoscopic approach*

For a long period of time, the only definitive resection of rectal cancer was through an open approach (LAR or APR). Beginning in the early 1990s, laparoscopic approaches have increasingly replaced open resections for colon resections due to better short-term outcomes and less surgical complications,<sup>33</sup> but rectal cancer is much

more challenging, primarily because of pelvic anatomical factors. Further, owing to the tumor's location in the pelvis, maintenance of resection margins is of greater concern. LS for rectal cancer, therefore, has not been universally accepted.<sup>34</sup> In the United States, laparoscopic rectal resection is performed in less than 20%<sup>35</sup> of the overall rectal resections and conversion rates to open surgery are high, ranging from 3% to 32%.<sup>36-41</sup>

#### *Laparoscopic surgery: technical considerations*

The laparoscopic approach follows the technique developed in open TME. As ASCRS guidelines recommend, LS for rectal cancer should follow standard oncologic principles: adequate distal margin, ligation at the origin of the arterial supply for the involved rectal segment, and mesorectal excision. Local excision is an appropriate treatment modality for carefully selected T1 rectal cancers without high-risk features. TME is recommended to use for curative resection of tumors of the middle and lower thirds of the rectum, either a part of low anterior or abdominoperineal resection. Appropriate surgical technique including sharp mesorectal excision and precise dissection which ensures en bloc removal is necessary to improve oncological outcome in rectal cancer surgery.<sup>5</sup>

As one of the common benefits of laparoscopy, LS provides the magnified views of the surgical planes which allows more precise dissection in rectal cancer patients. Compared to open surgery, LS provides more unprecedented, unobstructed views of the rectal dissection planes to not only for the surgeon but whole surgical team, which can even show more significant advantages in the patients with a narrow pelvis. Furthermore, the pneumoperitoneum can provide wide-open planes for mobilization of the mesorectum. On the other hand, there are several technical challenges in laparoscopic rectal cancer surgery. For instance, the difficulty to localize the tumor and obtain adequate exposure by laparoscopically retracting the rectum.

#### *Laparoscopic versus open approach; randomized controlled data*

Despite the advancements in LS during the last two decades, the equivalency between LS and open operation for rectal cancer has been remained in dispute. LS provides a similar resection but with better short term outcomes compared to open procedure. Several large clinical trials have shown that LS has lower morbidity rate and shorter hospitalization period.<sup>41-43</sup> An intact mesorectum and a negative circumferential margin (CRM) resection are associated with the lowest rates of locoregional recurrence and are considered important prognostic factors in rectal cancer. Several randomized trials have used these two factors as their primary outcomes, as short term surrogates for oncologic adequacy.<sup>44, 45</sup> Several randomized controlled trials have been published with conflicting results regarding to LS vs. open approaches.

The European MRC CLASICC Trial, was the first large multicenter randomized study that compared LS to open surgery for colon and rectal resections. They reported similar rates of positive resection margins between treatment groups except for patients who underwent laparoscopic anterior resection (LAR). Patients who underwent LAR had increased positive circumferential resection margin (CRM) rates compared to the open rectal cancer resection group.<sup>41</sup> A later publication reporting on three year follow up results showed that the observed higher positivity of the circumferential resection margin following LAR did not translate into an increased incidence of local recurrence.<sup>46</sup> Further, five year outcomes data also demonstrated no difference between LS and open rectal cancer groups in survival, disease-free survival, and local/regional recurrence.<sup>47</sup>

The American College of Surgeons Oncology Group (ACOSOG) Z6051 non-inferiority protocol was designed to determine the role of laparoscopic surgery in treating rectal cancer. ACOSOG Z6051 was a multicenter and randomized trial enrolling 486 patients with stage II or III rectal cancer within 12 cm of the anal verge that were randomly assigned to undergo laparoscopic or open surgery after neoadjuvant therapy. All the participating surgeons were credentialed based on video review and prior participation in surgical trials. The primary endpoint was a composite of pathologic outcome, defined as greater than 1 mm circumferential radial and distal margin plus an adequate TME. A successful resection occurred in 81.7 percent of LS and 86.9 percent of open resections, which did not demonstrate LS non-inferiority. The percentage of complete/nearly complete TME, negative distal margin, and negative CRM were higher in the open group compared to LS. Conversion rate to open resection was observed in 11% of LS patients. There was no significant difference in 30-days

readmission, serious morbidity, and length of stay between the two groups. ACOSOGZ6051 showed that among the stage II and III rectal cancer patients, LS failed to meet the criterion for non-inferiority compared to open resection in terms of pathologic outcomes. Oncologic outcomes have been compared in this trial, but the findings are in the pending status.<sup>45</sup>

The Australian Laparoscopic Cancer of the Rectum Trial (Ala CaRT), is another non-inferiority trial that was designed, like the ACOSOGZ6051 Trial, with similar endpoints, composite pathologic outcomes, and surgeon enrollment criteria. A total of 475 patients with stage T1 to T3 rectal cancer less than 15 cm from the anal verge were randomly assigned to laparoscopic or open resection. Analogous to ACOSOGZ6051, successful resection rate was lower in the LS compared to open surgery group (82% vs. 89%). The percentage of complete/nearly complete TME, negative distal margin, and negative CRM were higher in the open group compared to LS. In terms of surgical outcomes, return of bowel function was observed earlier in LS patients, and short term mortality was lower in the LS group as well. However, there were no significant differences in major postoperative complications between the two groups. Ala CaRT, like ACOSOGZ6051, showed that the laparoscopic approach is not established as non-inferior procedure compared to open resection.<sup>44</sup>

Another randomized trial was a South Korean trial (COREAN) started in 2009. The aim of this trial was to compare LS and open resection for patients with mid and low rectal cancer who underwent neoadjuvant chemotherapy. A total of 340 patients were randomly assigned into LS and open resection arms after preoperative chemoradiation therapy. Results revealed no significant differences between the two groups in terms of involvement of the circumferential resection margin, macroscopic quality of the TME specimen, number of harvested lymph nodes, or perioperative morbidity. Patients in the LS arm experienced less blood loss, earlier return of bowel function, decreased time to first defecation, and less amount of morphine prescription.<sup>48</sup>

Follow up publication with three-year results also showed that LS for locally advanced rectal cancer following neoadjuvant chemotherapy provides similar outcomes as open resection with respect to disease-free survival.<sup>49</sup>

Another European multi-center trial (Colorectal cancer Laparoscopic or Open Resection [COLORII]) started at the same time that ACOSOGZ6051 was initiated in the US. It is the largest randomized trial that has compared LS and open resection for rectal cancer. 1044 patients with a rectal cancer within 15 cm of the anal verge without any invasion or metastasis were randomly assigned to LS vs. open resection. T4 lesions or T3 lesions that were within 2 mm of the mesorectal fascia were excluded from the study. The primary endpoint was locoregional recurrence three years after index surgery and the secondary endpoints were disease free and overall survival. Macroscopic completeness of resection was lower in LS group compared to open but the difference was not statistically significant (88% vs. 92%,  $P=0.250$ ), and positive (<2 mm) circumferential resection margins were similar in both groups. In addition, the median distal margin, short term morbidity, and mortality rates were also similar. COLOR II results confirmed that minimally invasive approaches provide less blood loss, earlier return of bowel function, and shorter length of stay.<sup>50</sup> At three years, locoregional recurrence and survival were also similar between the two groups.<sup>51</sup> The proportion of CRM positivity was 22% in COLOR II Study, which is two times more than MRC CLASICC Trial (9%).<sup>47</sup> The COLOR II Trial clearly revealed that LS for rectal cancer is a non-inferior modality of performing proctectomy with curative intent. Furthermore, LS does not compromise oncologic outcomes and has some palpable advantages in terms of postoperative recovery, and may even provide some oncologic benefit in patients with more advanced disease. This trial established LS as the new standard of care in rectal cancer surgical treatment.<sup>52</sup>

### *Robotic resection of rectal cancer*

The first reported robotic surgery (RS) was performed by Cadiere for cholecystectomy in 1997.<sup>32</sup> Since that time, robotic approaches have been used in multiple surgical specialties, in particular in urological, cardiothoracic and

gynecological procedures.<sup>53</sup> However, colorectal robotic procedures are relatively new, and the first use of RS in colorectal diseases was reported in 2002.<sup>54</sup>

RS is an evolving surgical technique which seems to have the potential to overcome technical difficulties of conventional LS such as limited two-dimensional vision, restricted instrument motion and a very long learning curve. Utilizing RS allows a three-dimensional magnified vision, stable platform, high-dexterity maneuvers, and lower conversion rate to open surgery.<sup>55-57</sup> Due to these technical advancements and the ongoing development, robotics has seen increased application for low pelvic dissection, which claims to offer a better quality of TME dissection in addition to shorter (steeper) learning curves.<sup>58, 59</sup>

Data for robotic approaches to rectal cancer have recently been published and presented in several surgical and oncologic meetings revealing that RS is safe and comparable to the laparoscopic approach for rectal cancer resection. However, limitations for robotic approaches exist, including significantly higher cost, increased operative times, and limited number of well-experienced centers, which have limited the widespread adoption.<sup>60</sup>

### *Technical considerations of robotic surgery*

Currently there are two broadly accepted surgical approaches for robotic rectal resections; the hybrid technique and the total robotic technique. In the hybrid technique, surgeons utilize laparoscopic and robotic techniques, combined in different stages of the operation. One of the claimed advantages of this method is shorter operative time, where the splenic flexure and descending colon are mobilized by conventional laparoscopic technique followed by the robotic pelvic dissection.<sup>61-64</sup> Some surgeons use RS prior to LS in the combined method. Park *et al.* reported a combined RS plus LS called reverse-hybrid, performing the robotic lymphovascular (inferior mesenteric artery) and pelvic dissection before laparoscopic mobilization of the splenic flexure and descending colon.<sup>65</sup>

The other method is a totally robotic technique that is carried out entirely with robot assistance, which can be performed with single docking technique <sup>66-68</sup> or dual docking technique.<sup>69</sup>

### *Results of RS clinical trials*

In a single center randomized trial using the da Vinci surgical system, Baik *et al.* reported significantly higher conversion rate for laparoscopic low anterior resection compared to the robotic group (10.5 vs. 0.0%). Also, the serious complication rate was reported as 5.4% in the robotic group and 19.3% in the laparoscopic group. Mean length of stay was reported significantly shorter in RS compared to LS, which is comparable to the other published studies.<sup>70, 71</sup> Regarding the circumferential resection margin (CRM), no statistically difference was observed between groups, which is similar to another recent meta-analysis study reported CRM positivity from 1.5 to 4.5%, with no difference between the groups.<sup>72</sup> They concluded the feasibility and safety of robot-assisted tumor-specific mesorectal excision of rectal cancer in terms of oncologic outcomes.<sup>61</sup>

In another single center experience, Patrili *et al.* reported that robotic anterior rectal resection is a safe and feasible approach facilitating TME. They showed significantly shorter operative time in robotic rectal TME resection compared to the conventional LS. The conversion rate was significantly lower for RS. However, overall survival and disease-free survival were comparable between groups.<sup>73</sup>

Baek *et al.* published a case-matched study revealing that robotic TME may be as feasible and safe as laparoscopic resection in terms of technical and oncologic outcomes. Patients were included in the analysis from a prospectively maintained database. The patients were matched for gender, age, body mass index (BMI), and type of operative procedure. Patients received neoadjuvant chemoradiotherapy before undergoing surgery. The operation time was reported significantly shorter for robotic group. Also, conversion rate was lower in robotic arm. The anastomotic leak rate after surgery did not differ between two groups. In terms of negative margin, distal resection margins were negative in all surgical specimens.<sup>62</sup> Also, Baek reported CRM positivity for LS was more than double that for RS.

Park *et al.* also compared short-term outcomes and surgical quality of robot-assisted and laparoscopic TME in patients with low rectal cancer confirming safety and effectiveness of RS. Mean operation time was significantly shorter for LS group. Time to beginning regular diet and length of stay were similar in both groups. No significant differences were reported for distal resection margins, harvested lymph nodes, and circumferential margins between the two groups.<sup>74</sup> In another non-randomized, case control study evaluating 118 patients who underwent RS and LS, no differences were observed in lymph node yield, postoperative complications, and distal margin negativity, but CRM positivity (less than 2mm) was seen in one patient in RS arm compared to none in LS arm. The RS group had no conversion to open surgery compared to a 3.4% conversion rate seen with LS.<sup>68</sup>

Based on the review of several other small retrospective studies, robot-assisted rectal cancer resection has been deemed feasible, safe, and with no significant difference in CRM compared with open and laparoscopic approaches.<sup>63, 75-77</sup> Furthermore, a recently published article which reported on a prospective database of patients over a 7-year period, showed RS is safe and feasible for rectal cancer. The authors concluded that RS provides low conversion rate, satisfies all measures of pathologic adequacy, and offers acceptable oncologic outcomes. However, they emphasized that despite the promising data, results from properly sized randomized trials are required to make RS as a standard of care for rectal cancer patients.<sup>78</sup>

RObotic Versus LAParoscopic Resection for Rectal Cancer (ROLARR) is a large multicenter, prospective, randomized, controlled superiority trial which was designed to establish the superiority of robotic-assisted *versus* standard laparoscopic surgery for rectal cancer resections. The primary endpoint was intra operation conversion to open operation, and the key secondary endpoints were circumferential resection margin positivity rate, 3-year local recurrence, disease-free and overall survival rates and also operative morbidity and mortality, quality of life and cost-effectiveness. Preliminary data from the ROLARR Trial showed no significant difference between laparoscopic and robotic surgery regarding conversion to open and circumferential margin positivity; however, there was a trend toward improved outcomes with robotics for the most challenging patients including male, obese, and those with low tumors.<sup>79</sup> Unpublished (to date) results of the ROLARR Study, which were presented at the 2016 American Society of Colon and Rectal Surgeons (ASCRS) annual meeting, revealed that with respect to the primary endpoints, conversion rate was lower following robotic surgery, but no statistically significant evidence of superiority compared to laparoscopic surgery. Also regarding short-term oncological outcomes, CRM positivity rate was similar in both arms. 30-day complications and mortality rates were also reported similar in the two groups as well.<sup>80</sup>

#### *TaTME: the newer innovative approach for rectal cancer resection*

As we have discussed, technology and surgical technique developments have resulted in increasing use of minimally invasive techniques to perform TME. While not without controversy, careful review of the randomized controlled data from clinical trials suggests that laparoscopic resection for rectal cancer by experienced surgeons provides similar results to the open approach regarding perioperative morbidity and mortality, circumferential and distal resection margins involvement, quality of the surgical specimen, lymph node harvesting, local recurrence rates and overall survival.<sup>45, 47-51</sup> However, performing a laparoscopic TME is challenging because of a variety of factors including patient and tumor characteristics. In terms of patient factors, performing LS TME on an obese male patient with a narrow pelvis increases the risk of conversion to open TME.<sup>41, 50, 81</sup> Furthermore, the management of patients with bulky tumors in the anterior wall of the distal rectum using laparoscopic TME may cause an increased risk of surgical treatment failure owing to compromised circumferential resection margins.<sup>82</sup>

To conquer these difficulties, surgical investigators have been encouraged to find alternative techniques to successfully achieve better oncologic and surgical outcomes. Transanal TME (taTME) has been developed with consideration of the above issues and the fact that achieving macroscopic completeness of a resected rectal specimen is challenging according to patient anatomic factors and the quality of current surgical approaches. The taTME approach involves transanal establishment of the distal resection margin, establishment and dissection of



the TME plane from a “bottoms up” approach and laparoscopic assistance, and performance of abdominal portion of the LAR. In rectal cancer surgical treatment, the quality of the resected specimen (TME adequacy) is very important because it is correlated to oncologic outcomes.<sup>83</sup>

Lacy *et al.* has conducted the largest non-randomized controlled trial enrolling 140 patients undergoing TaTME.<sup>84</sup> The results of the study were very encouraging and promising in suggesting that this newly developed procedure is feasible and safe. Short-term morbidity and oncologic outcomes were comparable with other laparoscopic TME trials.<sup>44, 45, 50</sup> No conversion to open surgery was reported, which is in contrast to other laparoscopic TME studies and oncologic outcomes and CRM margins also compared favorably with those reported in previous laparoscopic TME trials. A currently planned prospective phase II US trial and a planned European RCT phase III (COLOR III) Trial will hopefully address the techniques’ safety and efficacy.

### Conclusions

Laparoscopic, robotic, transanal, and open approaches may all have certain indications in the management of rectal cancer. Reviewing all these clinical trials help us to understand the difficulties and technical challenges of rectal cancer surgical management. However, there is currently no solid or strong conclusion that can be reached regarding the superiority or inferiority of minimally invasive approaches relative to open surgery for rectal cancer.

Long-term follow up data, cost-effectiveness data and further randomized controlled trials are needed to precisely determine the role of the various minimally invasive approaches in the management of rectal cancer. Also, more-detailed meta-analyses are required to determine which factors lead to the best outcomes. It is likely that we will not end up with one procedure that is indicated for every patient, but rather the evolution of the various operations will allow us to customize the care of each patient. The approach for a female with BMI of 20 and a cancer in the mid/upper rectum will likely be different than the approach for a male patient with a BMI of 35 and a tumor just above the anal canal.

### References

1. Haggard FA, Boushey RP. Colorectal cancer epidemiology: incidence, mortality, survival, and risk factors. *Clin Colon Rectal Surg* 2009;22:191-7.
2. Siegel R, Ma J, Zou Z, Jemal A. Cancer statistics, 2014. *CA Cancer J Clin* 2014;64:9-29.
3. Minsky BD. Adjuvant therapy for rectal cancer--the transatlantic view. *Colorectal Dis* 2003;5:416-22.
4. van Gijn W, Marijnen CA, Nagtegaal ID, Kranenbarg EM, Putter H, Wiggers T, *et al.* Preoperative radiotherapy combined with total mesorectal excision for resectable rectal cancer: 12-year follow-up of the multicentre, randomised controlled TME trial. *Lancet Oncol* 2011;12:575-82.
5. Monson JR, Weiser MR, Buie WD, Chang GJ, Rafferty JF, Buie WD, *et al.* Practice parameters for the management of rectal cancer (revised). *Dis Colon Rectum* 2013;56:535-50.
6. Moghadamyeghaneh Z, Carmichael JC, Mills S, Pigazzi A, Nguyen NT, Stamos MJ. Variations in Laparoscopic Colectomy Utilization in the United States. *Dis Colon Rectum* 2015;58:950-6.
7. Kwon DS, Chang GJ. The role of minimally invasive surgery and outcomes in colorectal cancer. *Perm J* 2011;15:61-6.
8. Corman ML. Classic articles in colonic and rectal surgery. A method of performing abdominoperineal excision for carcinoma of the rectum and of the terminal portion of the pelvic colon: by W. Ernest Miles, 1869-1947. *Dis Colon Rectum* 1980;23:202-5.
9. Papagrigroriadis S. Transanal endoscopic micro-surgery (TEMS) for the management of large or sessile rectal adenomas: a review of the technique and indications. *Int Semin Surg Oncol* 2006;3:13.
10. Endreseth BH, Myrvold HE, Romundstad P, Hestvik UE, Bjerkeset T, Wibe A; Norwegian Rectal Cancer Group, *et al.* Transanal excision vs. major surgery for T1 rectal cancer. *Dis Colon Rectum* 2005;48:1380-8.
11. Chang AJ, Nahas CS, Araujo SE, Nahas SC, Marques CF, Kiss DR, *et al.* Early rectal cancer: local excision or radical surgery? *J Surg Educ* 2008;65:67-72.
12. Nivatvongs S. Surgical management of early colorectal cancer. *World J Surg* 2000;24:1052-5.
13. Buess GF, Raestrup H. Transanal endoscopic microsurgery. *Surg Oncol Clin N Am* 2001;10:709-31, xi.
14. Demartines N, von Flue MO, Harder FH. Transanal endoscopic microsurgical excision of rectal tumors: indications and results. *World J Surg* 2001;25:870-5.

15. Miles W. A method of performing abdomino-perineal excision for carcinoma of the rectum and of the terminal portion of the pelvic colon. *Lancet* 1908;1812-3.
16. Bordeianou L, Maguire LH, Alavi K, Sudan R, Wise PE, Kaiser AM. Sphincter-sparing surgery in patients with low-lying rectal cancer: techniques, oncologic outcomes, and functional results. *J Gastrointest Surg* 2014;18:1358-72.
17. Abraham NS, Davila JA, Rabeneck L, Berger DH, El-Serag HB. Increased use of low anterior resection for veterans with rectal cancer. *Aliment Pharmacol Ther* 2005;21:35-41.
18. Howell JD, Wotherspoon H, Leen E, Cooke TC, McArdle CS. Evaluation of a follow-up programme after curative resection for colorectal cancer. *Br J Cancer* 1999;79:308-10.
19. Ludwig KA. Sphincter-sparing resection for rectal cancer. *Clin Colon Rectal Surg* 2007;20:203-12.
20. Dixon CF. Anterior Resection for Malignant Lesions of the Upper Part of the Rectum and Lower Part of the Sigmoid. *Ann Surg* 1948;128:425-42.
21. Nelson H, Petrelli N, Carlin A, Couture J, Fleshman J, Guillem J, *et al.* Guidelines 2000 for colon and rectal cancer surgery. *J Natl Cancer Inst* 2001;93:583-96.
22. Wolmark N, Cruz I, Redmond CK, Fisher B, Fisher ER. Tumor size and regional lymph node metastasis in colorectal cancer. A preliminary analysis from the NSABP clinical trials. *Cancer* 1983;51:1315-22.
23. Nagtegaal ID, Quirke P. What is the role for the circumferential margin in the modern treatment of rectal cancer? *J Clin Oncol* 2008;26:303-12.
24. Tam IJ, Mohamdee MO, Martin IG, Scott N, Finan PJ, Johnston D, *et al.* Role of circumferential margin involvement in the local recurrence of rectal cancer. *Lancet* 1994;344:707-11.
25. Eald RJ, Ryall R. Recurrent cancer after restorative resection of the rectum. *Br Med J (Clin Res Ed)* 1982;284:826-7.
26. Beck DEWS, Hull TL, Roberts PI, Saclarides TJ, Senagore AJ, Stamos MJ, Steele SR. *The ASCRS Manual of Colon and Rectal Surgery*. Second edition: Springer; 2013.
27. Stewart DB, Dietz DW. Total mesorectal excision: what are we doing? *Clin Colon Rectal Surg* 2007;20:190-202.
28. Heald RJ, Husband EM, Ryall RD. The mesorectum in rectal cancer surgery--the clue to pelvic recurrence? *Br J Surg* 1982;69:613-6.
29. Maurer CA, Renzulli P, Kull C, Käser SA, Mazzucchelli L, Ulrich A, *et al.* The impact of the introduction of total mesorectal excision on local recurrence rate and survival in rectal cancer: long-term results. *Ann Surg Oncol* 2011;18:1899-906.
30. MacFarlane JK, Ryall RD, Heald RJ. Mesorectal excision for rectal cancer. *Lancet* 1993;341:457-60.
31. Arbmán G, Nilsson E, Hallbook O, Sjødahl R. Local recurrence following total mesorectal excision for rectal cancer. *Br J Surg* 1996;83:375-9.
32. Himpens J, Leman G, Cadiere GB. Telesurgical laparoscopic cholecystectomy. *Surg Endosc* 1998;12:1091.
33. Surgical C, Outcomes Assessment Program C, Kwon S, Billingham R, Farrokhi E, Florence M, Herzig D, *et al.* Adoption of laparoscopy for elective colorectal resection: a report from the Surgical Care and Outcomes Assessment Program. *J Am Coll Surg* 2012;214:909-918 e901.
34. Indar A, Efron J. Laparoscopic surgery for rectal cancer. *Perm J* 2009;13:47-52.
35. Kang CY, Halabi WJ, Luo R, Pigazzi A, Nguyen NT, Stamos MJ. Laparoscopic colorectal surgery: a better look into the latest trends. *Arch Surg* 2012;147:724-31.
36. Fleshman JW, Wexner SD, Anvari M, LaTulippe JF, Birnbaum EH, Kodner IJ, *et al.* Laparoscopic vs. open abdominoperineal resection for cancer. *Dis Colon Rectum* 1999;42:930-9.
37. Scheidbach H, Schneider C, Konradt J, Bärlechner E, Köhler L, Wittekind Ch, *et al.* Laparoscopic abdominoperineal resection and anterior resection with curative intent for carcinoma of the rectum. *Surg Endosc* 2002;16:7-13.
38. Feliciotti F, Guerrieri M, Paganini AM, De Sanctis A, Campagnacci R, Perretta S, *et al.* Long-term results of laparoscopic versus open resections for rectal cancer for 124 unselected patients. *Surg Endosc* 2003;17:1530-5.
39. Morino M, Giraudo G. Laparoscopic total mesorectal excision--the Turin experience. *Recent Results Cancer Res* 2005;165:167-79.

40. Leroy J, Jamali F, Forbes L, Smith M, Rubino F, Mutter D, *et al.* Laparoscopic total mesorectal excision (TME) for rectal cancer surgery: long-term outcomes. *Surg Endosc* 2004;18:281-9.
41. Guillou PJ, Quirke P, Thorpe H, Walker J, Jayne DG, Smith AM, *et al.* Short-term endpoints of conventional versus laparoscopic-assisted surgery in patients with colorectal cancer (MRC CLASICC trial): multicentre, randomised controlled trial. *Lancet* 2005;365:1718-26.
42. Veldkamp R, Kuhry E, Hop WC, Jeekel J, Kazemier G, Bonjer HJ, *et al.* Laparoscopic surgery versus open surgery for colon cancer: short-term outcomes of a randomised trial. *Lancet Oncol* 2005;6:477-84.
43. Fleshman J, Sargent DJ, Green E, Anvari M, Stryker SJ, Beart RW Jr, *et al.* Laparoscopic colectomy for cancer is not inferior to open surgery based on 5-year data from the COST Study Group trial. *Ann Surg* 2007;246:655-662; discussion 662-654.
44. Stevenson AR, Solomon MJ, Lumley JW, Hewett P, Clouston AD, Gebiski VJ, *et al.* Effect of Laparoscopic-Assisted Resection vs. Open Resection on Pathological Outcomes in Rectal Cancer: The ALaCaRT Randomized Clinical Trial. *JAMA* 2015;314:1356-63.
45. Fleshman J, Branda M, Sargent DJ, Boller AM, George V, Abbas M, *et al.* Effect of Laparoscopic-Assisted Resection vs. Open Resection of Stage II or III Rectal Cancer on Pathologic Outcomes: The ACOSOG Z6051 Randomized Clinical Trial. *JAMA* 2015;314:1346-55.
46. Jayne DG, Guillou PJ, Thorpe H, Quirke P, Copeland J, Smith AM, *et al.* Randomized trial of laparoscopic-assisted resection of colorectal carcinoma: 3-year results of the UK MRC CLASICC Trial Group. *J Clin Oncol* 2007;25:3061-8.
47. Jayne DG, Thorpe HC, Copeland J, Quirke P, Brown JM, Guillou PJ. Five-year follow-up of the Medical Research Council CLASICC trial of laparoscopically assisted versus open surgery for colorectal cancer. *Br J Surg* 2010;97:1638-45.
48. Kang SB, Park JW, Jeong SY, Nam BH, Choi HS, Kim DW, *et al.* Open versus laparoscopic surgery for mid or low rectal cancer after neoadjuvant chemoradiotherapy (COREAN trial): short-term outcomes of an open-label randomised controlled trial. *Lancet Oncol* 2010;11:637-45.
49. Jeong SY, Park JW, Nam BH, Kim S, Kang SB, Lim SB, *et al.* Open versus laparoscopic surgery for mid-rectal or low-rectal cancer after neoadjuvant chemoradiotherapy (COREAN trial): survival outcomes of an open-label, non-inferiority, randomised controlled trial. *Lancet Oncol* 2014;15:767-74.
50. van der Pas MH, Haglind E, Cuesta MA, Fürst A, Lacy AM, Hop WC, *et al.* Laparoscopic versus open surgery for rectal cancer (COLOR II): short-term outcomes of a randomised, phase 3 trial. *Lancet Oncol* 2013;14:210-8.
51. Bonjer HJ, Deijen CL, Abis GA, Cuesta MA, van der Pas MH, de Lange-de Klerk ES, *et al.* A randomized trial of laparoscopic versus open surgery for rectal cancer. *N Engl J Med* 2015;372:1324-32.
52. Hanna MH, Stamos MJ. Laparoscopic resection for rectal cancer: the new standard of care? *Translational Gastrointestinal Cancer* 2015;4:311-2.
53. Lanfranco AR, Castellanos AE, Desai JP, Meyers WC. Robotic surgery: a current perspective. *Ann Surg* 2004;239:14-21.
54. Weber PA, Merola S, Wasielewski A, Ballantyne GH. Telerobotic-assisted laparoscopic right and sigmoid colectomies for benign disease. *Dis Colon Rectum* 2002;45:1689-94; discussion 1695-1686.
55. Memon S, Heriot AG, Murphy DG, Bressel M, Lynch AC. Robotic versus laparoscopic proctectomy for rectal cancer: a meta-analysis. *Ann Surg Oncol* 2012;19:2095-101.
56. Lin S, Jiang HG, Chen ZH, Zhou SY, Liu XS, Yu JR. Meta-analysis of robotic and laparoscopic surgery for treatment of rectal cancer. *World J Gastroenterol* 2011;17:5214-20.
57. Yang Y, Wang F, Zhang P, Shi C, Zou Y, Qin H, *et al.* Robot-assisted versus conventional laparoscopic surgery for colorectal disease, focusing on rectal cancer: a meta-analysis. *Ann Surg Oncol* 2012;19:3727-36.
58. Pai A, Melich G, Marecik SJ, Park JJ, Prasad LM. Current status of robotic surgery for rectal cancer: A bird's eye view. *J Minim Access Surg* 2015;11:29-34.
59. Hellan M, Ouellette J, Lagares-Garcia JA, Rauh SM, Kennedy HL, Nicholson JD, *et al.* Robotic Rectal Cancer Resection: A Retrospective Multicenter Analysis. *Ann Surg Oncol* 2015;22:2151-8.
60. Champagne BJ, Makhija R. Minimally invasive surgery for rectal cancer: are we there yet? *World J Gastroenterol* 2011;17:862-6.

61. Baik SH, Kwon HY, Kim JS, Hur H, Sohn SK, Cho CH, *et al.* Robotic versus laparoscopic low anterior resection of rectal cancer: short-term outcome of a prospective comparative study. *Ann Surg Oncol* 2009;16:1480-7.
62. Baik JH, Pastor C, Pigazzi A. Robotic and laparoscopic total mesorectal excision for rectal cancer: a case-matched study. *Surg Endosc* 2011;25:521-5.
63. Fernandez R, Anaya DA, Li LT, Orcutt ST, Balentine CJ, Awad SA, *et al.* Laparoscopic versus robotic rectal resection for rectal cancer in a veteran population. *Am J Surg* 2013;206:509-17.
64. Bianchi PP, Ceriani C, Locatelli A, Spinoglio G, Zampino MG, Sonzogni A, *et al.* Robotic versus laparoscopic total mesorectal excision for rectal cancer: a comparative analysis of oncological safety and short-term outcomes. *Surg Endosc* 2010;24:2888-94.
65. Park IJ, You YN, Schlette E, Nguyen S, Skibber JM, Rodriguez-Bigas MA, *et al.* Reverse-hybrid robotic mesorectal excision for rectal cancer. *Dis Colon Rectum* 2012;55:228-33.
66. Kim JC, Yang SS, Jang TY, Kwak JY, Yun MJ, Lim SB. Open versus robot-assisted sphincter-saving operations in rectal cancer patients: techniques and comparison of outcomes between groups of 100 matched patients. *Int J Med Robot* 2012;8:468-75.
67. Leong QM, Son DN, Cho JS, Baik SJ, Kwak JM, Amar AH, *et al.* Robot-assisted intersphincteric resection for low rectal cancer: technique and short-term outcome for 29 consecutive patients. *Surg Endosc* 2011;25:2987-92.
68. Kwak JM, Kim SH, Kim J, Son DN, Baik SJ, Cho JS. Robotic vs. laparoscopic resection of rectal cancer: short-term outcomes of a case-control study. *Dis Colon Rectum* 2011;54:151-6.
69. Kang J, Yoon KJ, Min BS, Hur H, Baik SH, Kim NK, *et al.* The impact of robotic surgery for mid and low rectal cancer: a case-matched analysis of a 3-arm comparison--open, laparoscopic, and robotic surgery. *Ann Surg* 2013;257:95-101.
70. Park JS, Choi GS, Lim KH, Jang YS, Jun SH. S052: a comparison of robot-assisted, laparoscopic, and open surgery in the treatment of rectal cancer. *Surg Endosc* 2011;25:240-8.
71. Kim NK, Kang J. Optimal Total Mesorectal Excision for Rectal Cancer: the Role of Robotic Surgery from an Expert's View. *J Korean Soc Coloproctol* 2010;26:377-87.
72. Trastulli S, Farinella E, Cirocchi R, Cavaliere D, Avenia N, Sciannameo F, *et al.* Robotic resection compared with laparoscopic rectal resection for cancer: systematic review and meta-analysis of short-term outcome. *Colorectal Dis* 2012;14:e134-156.
73. Patrìti A, Ceccarelli G, Bartoli A, Spaziani A, Biancafarina A, Casciola L. Short- and medium-term outcome of robot-assisted and traditional laparoscopic rectal resection. *JLS*. 2009;13:176-83.
74. Park JS, Choi GS, Lim KH, Jang YS, Jun SH. Robotic-assisted versus laparoscopic surgery for low rectal cancer: case-matched analysis of short-term outcomes. *Ann Surg Oncol* 2010;17:3195-202.
75. deSouza AL, Prasad LM, Ricci J, Park JJ, Marecik SJ, Zimmermann A, *et al.* A comparison of open and robotic total mesorectal excision for rectal adenocarcinoma. *Dis Colon Rectum* 2011;54:275-82.
76. Lee SH, Lim S, Kim JH, Lee KY. Robotic versus conventional laparoscopic surgery for rectal cancer: systematic review and meta-analysis. *Ann Surg Treat Res* 2015;89:190-201.
77. Popescu I, Vasilescu C, Tomulescu V, Vasile S, Sgarbura O. The minimally invasive approach, laparoscopic and robotic, in rectal resection for cancer. A single center experience. *Acta Chir Iugosl* 2010;57:29-35.
78. Pai A, Marecik SJ, Park JJ, Melich G, Sulo S, Prasad LM. Oncologic and Clinicopathologic Outcomes of Robot-Assisted Total Mesorectal Excision for Rectal Cancer. *Dis Colon Rectum* 2015;58:659-67.
79. Collinson FJ, Jayne DG, Pigazzi A, Tsang C, Barrie JM, Edlin R, *et al.* An international, multicentre, prospective, randomised, controlled, unblinded, parallel-group trial of robotic-assisted versus standard laparoscopic surgery for the curative treatment of rectal cancer. *Int J Colorectal Dis* 2012;27:233-41.
80. Pigazzi A. Robotic versus Laparoscopic Resection for Rectal Cancer (ROLARR Trial). Los Angeles, USA: American Society of Colon and Rectal Surgeons (ASCRS) Annual Meeting; 2016.
81. Araujo SE, da Silva e Sousa AH Jr, de Campos FG, Habr-Gama A, Dumarco RB, Caravatto PP, *et al.* Conventional approach x laparoscopic abdominoperineal resection for rectal cancer treatment after neoadjuvant chemoradiation: results of a prospective randomized trial. *Rev Hosp Clin Fac Med Sao Paulo* 2003;58:133-40.

82. Velthuis S, van den Boezem PB, van der Peet DL, Cuesta MA, Sietses C. Feasibility study of transanal total mesorectal excision. *Br J Surg* 2013;100:828-831; discussion 831.
83. Nagtegaal ID, van de Velde CJ, van der Worp E, Kapiteijn E, Quirke P, van Krieken JH, *et al.* Macroscopic evaluation of rectal cancer resection specimen: clinical significance of the pathologist in quality control. *J Clin Oncol* 2002;20:1729-34.
84. Lacy AM, Tasende MM, Delgado S, Fernandez-Hevia M, Jimenez M, De Lacy B, *et al.* Transanal Total Mesorectal Excision for Rectal Cancer: Outcomes after 140 Patients. *J Am Coll Surg* 2015;221:415-23.

*Conflicts of interest.*—The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Article first published online: July 15, 2016.