The feasibility of laparoscopic surgery was highlighted by more than 24 randomized, controlled trials (RCTs) including 5 level I RCTs in the previous review with mostly consistent results. Only the UK CLASICC trial (Conventional Versus Laparoscopic-assisted Surgery in Patients with Colorectal Cancer), which included patients with rectal cancer, noted an insignificantly increased rate of positive circumferential margins in the laparoscopic cohort without an increase in long-term tumor recurrence. Since the last review, 14 additional RCTs and metaanalyses on laparoscopic surgery for colon cancer have confirmed the short-term benefits and oncologic noninferiority to the open approach. This includes a metaanalysis (including 23 RCTs and 20...
systematic reviews for RCTs) and the Australasian Laparoscopic Colon Cancer Study Trial. In total, laparoscopic surgery compared with open surgery had been shown to be technically feasible with multiple short-term benefits (less blood loss, less narcotics use, earlier return of bowel function, and decreased duration of hospital stay), similar or noninferior oncologic outcomes (lymph node retrieval, margins, overall survival [OS], disease-free survival [DFS]), and lower rates of incisional hernia and adhesive small bowel obstruction. As such, laparoscopic colectomy for colon cancer should currently be considered an acceptable alternative to an open resection in the hands of experienced surgeons. Only 1 RCT has investigated a robotic approach compared with laparoscopic colectomy for right-sided tumors with the robotic approach providing few benefits (similar pain, hospital stay, complication rates, and pathologic outcomes) to justify the greater cost and longer duration. Thus, the robotic approach does not currently have RCT data to justify use over laparoscopic surgery.

Historical RCTs have demonstrated no oncologic benefit with the no-touch technique, high ligation of the inferior mesenteric artery and an increased radiologically detected leak rate with hand-sewn compared with stapled anastomosis. Since the last review, an RCT compared iso-versus antiperistaltic stapled side-to-side anastomosis (SSSA) and showed no significant difference in outcomes, but was suspended after detecting increased morbidity in the isoperistaltic SSSA group (which had the only two anastomotic leaks). An RCT demonstrated no difference in terms of infection rates between subcuticular and interrupted suture closure of clean-contaminated wounds after colon cancer resection. Specimen extraction through the anus versus mini-laparotomy showed no significant difference in terms of operative time, blood loss or length of hospital stay with the exception of less postoperative pain and no infections in the former group.

**Endoscopic Stent for Colonic Obstruction**

For the purposes of this review, we will focus on the role of colonic stents (SEMS) in avoiding surgery at the time of emergent bowel obstruction. The majority of literature on this subject is nonrandomized with very few RCTs and conflicting results. A systematic review of uncontrolled trials and case reports on SEMS revealed a clinical success rate of 72% when used as bridge to surgery and uncommon major complications. These results were not supported by the first RCT on this topic (Stent-In 2 trial) which revealed stent-related perforations in 13%–23% of patients and a higher risk of cancer recurrence if a perforation occurred. This raised long-term oncologic apprehension, but a metaanalysis of four RCT’s and seven subsequent RCTs suggested similar cumulative mortality rates after stenting as a bridge to surgery versus surgery alone. Interestingly, while overall stoma rates differed significantly in favor of SEMS, the permanent stoma rates were similar.

Based on the available RCT data, the use of SEMS is associated with a higher rate of a successful primary anastomosis, lower rate of short-term colostomy requirement and avoids the need for a second procedure for colostomy reversal. The length of stay for SEMS placement and elective surgery (within 1–2 weeks) is also shorter than that for emergency surgery. This makes SEMS an attractive option despite the higher than anticipated perforation rate, noting that OS is not negatively impacted.

**Primary Tumor Resection in Setting of Metastatic Disease**

Current guidelines limit primary tumor resection (PTR) in the presence of metastatic disease (mCRC) to symptomatic patients, which is supported by literature. However, the role of PTR in asymptomatic patients to avoid future symptoms or improve survival is controversial. No RCTs have currently addressed this topic but two trials are
ongoing. A retrospective analysis of two RCTs with a different aim\textsuperscript{14,15} and 22 nonrandomized studies showed significantly better survival for the PTR group. However, these studies have inherent biases and are thus inconclusive. Improving survival despite decreasing incidence of PTR could be due to improved systemic therapy use. Until the ongoing RCTs conclude,\textsuperscript{12,13} a nonoperative approach in the absence of symptoms is recommended in accordance with NCCN guidelines.

**Perioperative Care/Enhanced Recovery After Surgery**

These clinical pathways were developed to accelerate recovery after surgery and include perioperative interventions focusing on anesthesia, multimodal narcotic-sparing analgesia, reduction of surgical stress, goal-directed fluid therapy, prevention of nausea and ileus, thromboembolic prophylaxis, minimally invasive techniques, early nutrition and early mobilization. A total of 16 RCTs and two metaanalysis of RCTs have been published on this topic.\textsuperscript{1,16,17} Results indicate earlier return of bowel function, shorter hospital stay, and decreased overall morbidity without an increase in readmission rates or surgical complications.\textsuperscript{16,17} The randomized LAFA trial demonstrated sustained superiority of ERAS pathway for colon cancer patients undergoing laparoscopic surgery compared with open surgery.\textsuperscript{18} Thus, implementation of ERAS pathways in colon cancer patients has led to shorter hospital stays (by 2–3 days) and decreased morbidity without an increase in the readmission rate and should be implemented nationwide.

**Postoperative Surveillance Schedules**

Prior to the last review, 5 RCTs compared surveillance strategies for early diagnosis of cancer recurrence\textsuperscript{1} and failed to show a survival difference with intensive surveillance. Of the several large RCTs published since then, we chose three as level I evidence: FACS, CEAWatch and GILDA trials.\textsuperscript{19–21} All of these failed to show an OS benefit with intensive regimens, despite earlier detection of recurrences that were treated with curative intent. Another RCT looking at this question is ongoing.\textsuperscript{22} In summary, published RCTs do not demonstrate an OS advantage with intensive surveillance regimens despite DFS improvement.

**Adjuvant Therapy**

Prior to the last review, adjuvant chemotherapy (intravenous fluoropyrimidine (FP) monotherapy) for 6 months was associated with improved survival in patients with stage III and possibly high-risk stage II colon cancer patients. Subsequent studies tested the noninferiority of oral FP alternatives and benefit of FP-based polychemotherapy and confirmed that capecitabine is equivalent to infusional 5-fluorouracil (5-FU)\textsuperscript{3} and that the addition of oxaliplatin to either infusional or oral FP therapy is superior to monotherapy with FP alone.\textsuperscript{1,23,24} The role of adjuvant therapy for stage II disease remains controversial with no additional RCTs to address this issue since the last review.

Biologic-targeted therapies, cetuximab (cmab) and bevacizumab (bev) have been shown to improve outcomes when combined with chemotherapy in mCRC. However cmab added to adjuvant FOLFOX for resected stage III colon cancer failed to show a benefit, rather a trend toward harm was noted in the US NCI-based study.\textsuperscript{25} Similarly, the addition of bev to polychemotherapy in another US NCI-based study showed no benefit.\textsuperscript{26} Given early separation of survival curves in favor of bev, an RCT is currently testing the benefit of expanded duration anti-VEGF therapy (regorafenib) after completion of standard adjuvant therapy (NCT02664077). While 6 months of adjuvant therapy is currently the standard of care, an ongoing global study (IDEA Study) is assessing the
noninferiority of 3 versus 6 months of postoperative adjuvant chemotherapy. Initial results failed to demonstrate statistical non-inferiority with continued analysis ongoing.27

RECTAL CANCER

Rectal cancer is managed in a multimodality fashion, with surgery continuing to be the cornerstone for cure. Total mesorectal excision (TME) continues to be the gold standard for surgical excision but has never been tested in an RCT. TME alone leads to lower rates of local recurrence (LR), now ranging from 3% to 7%, and increased DFS. However, distant recurrences remain problematic.

Surgical Approach and Techniques

The last review included several trials but the findings of the rectal cancer subset of patients in the UK-CLASICC trial who underwent TME and had a higher rate of positive circumferential margin (CRM) in the laparoscopic group is worth mentioning. However, this did not translate into significant long-term differences in rates of LR, 3-year DFS, or OS.2 Since then, 10 RCTs have been published on this topic and four are being presented as level 1 evidence below.27-30 Both the COREAN30 and COLOR II trial29 compared laparoscopic to open rectal cancer resections and showed no difference in the quality of the oncologic resection, complication rates and long-term survival outcomes. However, both trials had limitations such as nonobese population, involvement limited to 3 tertiary centers with experienced surgeons, and low complete mesorectal excision rate (73%) in the COREAN trial. Similarly, the COLOR II trial used neoadjuvant therapy in stage I patients, had low rate of pathologic complete response (pCR), high rate for CRM involvement for tumors located in the low rectum (22%) in the open group and a high permanent stoma rate (29%) in the laparoscopic group. Since the above two trials, two major well-done large RCTs have been published on this topic; ACOSOG-Z605128 and ALaCaRT trial27 which are highlighted in Table 1. Both trials failed to show noninferiority of the laparoscopic approach compared with open surgery for pathologic outcomes. In all four trials, the laparoscopic group had significantly longer operative time, less blood loss, quicker return of bowel function and two trials demonstrated a shorter hospital stay. In summary, the available RCT data do not support the use of laparoscopic resection in patients with rectal cancer at this time. The ROLARR trial, the only large RCT, comparing robotic-assisted and laparoscopic surgery for curable rectal cancer is currently under way. At the time of the last unpublished report,31 no significant differences were noted between groups.

A few additional RCTs have looked at various aspects of rectal cancer resection as below. The French GRECCAR III trial demonstrated higher infectious morbidity for rectal cancer surgery without mechanical bowel preparation (MBP).32 The role of diverting loop ileostomies (DLI) with low anterior resection (LAR) has been studied in three large RCTs and a pooled analysis of RCT’s.33-35 All found a lower incidence of anastomotic leaks when DLI was performed.

Three RCTs have also explored surgical approaches to improve the quality of the distal resection in low rectal cancer. We review one of the two on sphincter saving procedures36 and the only one on abdominoperineal resection (APR) patients below.37 Transanal/perineal dissection of the distal LAR specimen resulted in a significant decrease in CRM positivity rate compared with laparoscopic dissection.36 Extralevator (cylindrical) APR in prone position demonstrated a lower LR rate compared with conventional APR in a lithotomy position but also had a higher complication rate.
Together, these trials highlight the need for a better surgical approach for the distal portion of the dissection. While we continue to investigate optimization of sphincter saving procedures, cylindrical APR is recommended to decrease the incidence of a positive CRM and associated morbidity.

Reconstructive Techniques

Eight RCTs (including some prior to the last review) have shown the functional superiority and decreased complication rate (leak and strictures) with colonic J-pouches (CJP) over straight anastomosis. Three RCTs (two prior to the last review) compared CJs to side-to-end anastomosis and found similar functional outcomes. Comparison of 3-cm and 6-cm side limb sizes in a side-to-end anastomosis revealed no difference, but the study was underpowered. Six RCTs (5 prior to last review) compared CJs with transverse coloplasty pouches (TCPs) showing better functional outcomes with CJs in two trials but comparable outcomes in the other four trials. This contradicts previous reports suggesting a higher leak rate with TCP. Data suggests that a straight end-to-end anastomosis has the poorest functional outcome. Due to lack of added functional benefit and ease of creation, a side-to-end anastomosis appears to be a good alternative to CJP.

Organ Preservation

The last review discussed two RCTs on this subject looking at cT1N0 and cT2N0 lesions separately. Both compared transanal endoscopic microsurgery (TEM) to TME with no difference in rates of R0 resection, LR or DFS. However, both studies were underpowered with inadequate long-term follow-up considering the high rates of LR noted in multiple large retrospective data sets. Although, level 1 evidence to define the role of organ preservation is currently deficient, nonrandomized studies have shown organ preservation rates of greater than 75% with cT1-2N0 tumors and rates of 50% with cT3N0 tumors. Appropriate patient selection and follow up is critical. Of particular mention in this ‘watch and wait’ approach is Angelita Habr-Gama and her group in San Paulo who have published their largest and longest experience. They deliver three cycles of chemotherapy after chemoradiotherapy (CRT) before reassessment at 10 weeks with a strict definition of clinical complete response (cCR). Patients with suspicious areas undergo full-thickness local excision. Only 10% to 20% of cases show a cCR (including T2-3,N0-1 lesions) with LR rates of 10% to 30% and the vast majority amenable to salvage resection. A current RCT (NCT02008656) is assessing the possibility of organ preservation in patients with cCR in the setting of total neoadjuvant therapy (TNT).

Neoadjuvant Radiotherapy

The last review highlighted eight trials showing a decrease in LR with radiotherapy (XRT) administered either preoperatively or postoperatively. Of these, the Dutch trial underscored the benefit of preoperative XRT even when optimal TME surgery was performed. One RCT showed an improvement in OS with preoperative XRT but most studies have not replicated this finding. No RCT has added to this topic since the last review.

Prior to the last review, the CAO/ARO/AIO 94 trial randomized patients to pre- or postoperative long-course chemoradiation (LC-CRT). Results showed less toxicity and improved 5- and 10-year LR rate in the preoperative chemoradiation group with no difference in OS or DFS. Another RCT compared preoperative short-course radiotherapy (SC-XRT) followed by surgery (within 7 days) to surgery with selective postoperative LC-CRT (for CRM positive patients). Short- and long-term local
<table>
<thead>
<tr>
<th>Trial</th>
<th>Inclusion Criteria/on</th>
<th>Primary Endpoint</th>
<th>Successful Resection</th>
<th>Negative CRM</th>
<th>Clear Distal Margin</th>
<th>Complete or Near-Complete TME</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kang et al, 2010</td>
<td>Stage II-III tumors within 9 cm of verge/340 patients</td>
<td>3-y DFS rate</td>
<td>—</td>
<td>97.1% lap vs 95.9% open ($P = .77$)</td>
<td>100% lap vs 100% open ($P = .54$)</td>
<td>91.8% lap vs 88% open ($P = .41$)</td>
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<td>• OR time: 245 min lap vs 197 min open</td>
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<td>• EBL: 200 mL lap vs 217 mL open</td>
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<td>• ROBF: 38 h lap vs 60 h open</td>
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<td></td>
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<td>• Hospital stay: 8 d lap vs 9 d open</td>
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<td>• Conversion rate: 1.5%</td>
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<tr>
<td>Van der Pas et al, 2013</td>
<td>T1-T3 tumors within 15 cm of verge/1044 patients</td>
<td>3-y LR rate</td>
<td>—</td>
<td>90% lap vs 90% open ($P = .85$)</td>
<td>100% lap vs 100% open ($P = .67$)</td>
<td>97% lap vs 98% open ($P = .25$)</td>
<td>• 3-y LR, DFS, OS: Similar</td>
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<td>• OR time: 240 min lap vs 188 min open</td>
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<td>• ROBF: 2 d lap vs 3 d open</td>
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<td>• Hospital stay: 8 d lap vs 9 d open</td>
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<td>• Conversion rate: 17%</td>
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<tr>
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<td>Criteria</td>
<td>Laparoscopic vs Open</td>
<td>P Value</td>
<td>Conversion Rate</td>
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<tr>
<td>Stevenson et al, 2015</td>
<td>T1-T3 tumors within 15 cm</td>
<td>Meeting all the following criteria: Complete TME, CRM ≥1 mm and distal</td>
<td>82% lap vs 89% open</td>
<td>.06</td>
<td>9%</td>
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<tr>
<td></td>
<td>of rectum/475 patients</td>
<td>margin ≥1 mm</td>
<td>93% lap vs 97% open</td>
<td>.91</td>
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<td></td>
<td></td>
<td></td>
<td>98% lap vs 98% open</td>
<td>.06</td>
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<td></td>
<td>97% lap vs 99% open</td>
<td>.91</td>
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<tr>
<td>Fleshman et al, 2015</td>
<td>Stage II-III tumors within 12 cm of rectum/248 patients</td>
<td>Composite of CRM &gt;1 mm, negative distal margin and completeness of TME</td>
<td>81.7% lap vs 86.9% open</td>
<td>.11</td>
<td>11.3%</td>
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<td></td>
<td>87.9% lap vs 92% open</td>
<td>.67</td>
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<td></td>
<td></td>
<td>99% lap vs 99% open</td>
<td>.20</td>
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Abbreviations: CRM, circumferential margin; DFS, disease-free survival rate; EBL, estimated blood loss; lap, laparoscopic; LR, local recurrence rate; OR time, operative time; OS, overall survival rate; ROBF, return of bowel function; TME, total mesorectal excision.
control and DFS were significantly improved in the preoperative treatment group with similar OS. Neoadjuvant XRT leads to fewer LR, less toxicity and postoperative complications without an effect on survival.

Two trials have directly compared preoperative SC-XRT (surgery within 7 days) with LC-CRT (surgery in 4–6 weeks) and showed no difference in LR or long-term DFS or OS between treatment groups. Subgroup analysis of the Trans-Tasman trial revealed a significant benefit of treating low rectal cancer (<5 cm) with LC-CRT in terms of LR, which is consistent with the Dutch trial results. Another RCT revealed greater tumor downstaging with neoadjuvant LC-CRT compared with SC-XRT but with no difference in the R0 resection rates. Thus, both SC-XRT and LC-CRT have similar rates of LR, DFS and OS with LC-CRT offering greater tumor downstaging. At present, SC-XRT has gained favor in Europe but not in the US, likely due to differences in practice patterns and reimbursement.

The optimal timing of surgery following neoadjuvant therapy has been evaluated in two RCTs. The Lyon trial (surgery within 6–8 weeks after neoadjuvant therapy completion) demonstrated increased clinical response and pCR rate compared with a 2 week delay. However, this did not translate into improved rates of long-term LR, DFS or OS. The second trial increased the interval further by comparing surgery at either 7 or 11 weeks after LC-CRT. The 11 week group had no increase in the pCR rate but had higher morbidity and more difficult surgical resection. A Polish trial compared early (7–10 days) versus delayed surgery (4–5 weeks) after SC-XRT and showed similar results with more downstaging in the delay group but no effect on rates of R0 resection, LR and OS. These results are reinforced by the interim analysis of the ongoing Stockholm III trial. In total, RCTs support surgical resection more than 6 to 8 weeks after neoadjuvant XRT due to more downstaging and higher pCR rate, but a survival benefit is unproven. Moreover, the above studies use pCR as a primary endpoint, which is a poor surrogate for DFS and OS.

**Chemotherapy as a Radiation Sensitizer**

Previous RCTs have demonstrated that the combined modality of CRT leads to improved LR rates compared with XRT alone but does not impact OS, thus supporting the addition of FP chemotherapy (5-FU and LV) to XRT. Several small studies have suggested a further improvement in pCR and downstaging with the addition of oxaliplatin to FP when given with neoadjuvant CRT. The NCI NSABP R-04 study formally evaluated the substitution of oral capecitabine (cape) for infusional 5-FU (CVI 5-FU) as well as intensification of radiosensitization by adding oxaliplatin. Over 1500 patients were randomized into one of four neoadjuvant CRT arms. Local control, surgical downstaging and pCR rates were similar between the cape and CVI 5-FU arms. However, the addition of oxaliplatin failed to improve rates of DFS, OS, pCR, surgical downstaging or sphincter-sparing surgery. Five other RCTs confirmed that cape was an acceptable replacement for 5-FU and that adding oxaliplatin to CRT offered only toxicity. The incorporation of irinotecan, cetuximab, panitumumab and bevacizumab has been explored in small studies suggesting increased downstaging, but larger RCTs are awaited.

**Chemotherapy for Systemic Disease Control**

Five RTCs and a metaanalysis have attempted to demonstrate a survival advantage with adjuvant chemotherapy but only one succeeded. However, most studies had limitations of inconsistent clinical staging, underpowering and limited compliance with heterogenous chemotherapy regimens. A metaanalysis confirmed nearly 1/3rd of patients in most RCTs did not receive intended adjuvant treatment. A 14%
Increase in mortality was reported for each 4-week delay in starting adjuvant therapy, after a 4-week postoperative interval. In part due to the limited data, current consensus guidelines continue to recommend 4 months of adjuvant FP-based chemotherapy either pre- or postoperatively, independent of those receiving neoadjuvant XRT. Early RCT data suggests that preoperative chemotherapy may be more effectively delivered, better tolerated without compromising surgical outcomes and possibly leads to additional downstaging for selective elimination of radiotherapy or surgery. The NCI-NCTN PROSPECT study (NCT01515787) is an ongoing RCT testing if preoperative XRT can be excluded in some patients when objective tumor regression is seen with neoadjuvant chemotherapy alone.

The RCTs that follow do not represent all trials that have contributed to our current knowledge of the optimal care for the patient with colon or rectal cancer. Rather, we have highlighted those trials that have helped define the standard of care in 2017. Only RCTs published in a peer-reviewed format are considered.


This trial investigated whether the short-term benefits associated with laparoscopic-assisted colon resection (LCR) compared with open colon resection (OCR) could be achieved safely, without survival disadvantages. A total of 587 of 601 eligible patients with potentially curable colon cancer were randomized to receive LCR or OCR. Primary endpoints were 5-year OS, recurrence-free survival, and freedom from recurrence rates, compared using an intention-to-treat analysis. With 5-year confirmed follow-up data for survival and recurrence on 567 (96.6%), there were no significant differences between the LCR and OCR groups in 5-year follow-up of OS (77.7% vs 76.0%, P = .64), recurrence-free survival (72.7% vs 71.2%, P = .70), or freedom from recurrence (86.2% vs 85.6%, P = .85). With long-term follow-up, this study demonstrated that LCR was not inferior to OCR in direct measures of survival and disease recurrence.


This study randomized patients with malignant colonic obstruction to emergency surgery or stent placement as a bridge to elective surgery with an aim to compare the oncological outcomes. Of 98 patients included in the original Stent-In 2 trial, patients with benign (16) or incurable (23) disease were excluded from this analysis study, along with a patient who had withdrawn from the trial. Of the remaining 58 patients, 32 were randomized to emergency surgery (31 resection, 1 stoma only) and 26 to stenting. Unsuccessful stenting required emergency surgery in six patients owing to wire or stent perforation. Locoregional or distant disease recurrence developed in nine of 32 patients in the emergency surgery group and 13 of 26 in the stent group. DFS was worse in the subgroup with stent- or guidewire-related perforation. Five of six patients in this subgroup developed a recurrence, compared with nine of 32 in the emergency surgery group and eight of 20 who had unperforated stenting. The authors concluded that there is not enough evidence to strongly refute the approach.

This RCT investigated which perioperative treatment (fast track [FT] or standard care), is the optimal approach for patients undergoing segmental laparoscopic or open resection for colon cancer. Patients eligible for segmental colectomy were randomized to laparoscopic or open colectomy, and to FT or standard care, resulting in 4 treatment groups. Primary outcome was total postoperative hospital stay (THS). Secondary outcomes were postoperative hospital stay (PHS), morbidity, reoperation rate, readmission rate, in-hospital mortality, quality of life at 2 and 4 weeks, patient satisfaction and in-hospital costs. Median THS in the laparoscopic/FT group was 5 (interquartile range: 4–8) days; open/FT 7 (5–11) days; laparoscopic/standard 6 (4.5–9.5) days, and open/standard 7 (6–13) days ($P<.001$). Median PHS in the laparoscopic/FT group was 5 (4–7) days; open/FT 6 (4.5–10) days; laparoscopic/standard 6 (4–8.5) days and open/standard 7 (6–10.5) days ($P<.001$). Secondary outcomes did not differ significantly among the groups. Regression analysis showed that laparoscopy was the only independent predictive factor to reduce hospital stay and morbidity. Optimal perioperative treatment for patients requiring segmental colectomy for colon cancer is laparoscopic resection embedded in an FT program. If open surgery is performed, it is also preferentially done in FT care.


This RCT aimed to determine the value of frequent Carcino-Embryonic Antigen (CEA) measurements and CEA-triggered imaging for detecting recurrent disease after definitive therapy for colon cancer. Participating sites were sequentially assigned an alternating change from their usual follow-up care to an intensified follow-up schedule of CEA measurements every 2 months with imaging in case of two CEA rises. The primary outcomes were the proportion of recurrences that could be treated with curative intent, recurrences with definitive curative treatment outcome, and the time to detection of recurrent disease. In the 3223 patients that were included; 243 recurrences were detected (7.5%). A higher proportion of recurrences were detected in the intervention protocol compared with the control protocol (OR = 1.80; 95%-CI: 1.33–2.50; $P = .0004$) as well as the proportion of recurrences that could be treated with curative intent (OR = 2.84; 95%-CI: 1.38–5.86; $P = .0048$) and were treated with curative treatment (OR = 3.12, 95%-CI: 1.25–6.02, $P$-value: 0.0145). The time to detection of recurrent disease was significantly shorter in the intensified follow-up protocol (HR = 1.45; 95%-CI: 1.08–1.95; $P = .013$). However, OS and DFS endpoints have not yet been reported.


This RCT sought to determine whether laparoscopic (lap) resection is noninferior to open resection for patients with stage II or III rectal cancer as determined by gross pathologic and histologic evaluation of the resected proctectomy specimen. The trial was conducted by credentialled surgeons from 35 institutions in
and comprised a total of 486 patients. The primary outcome assessing efficacy was a composite of CRM greater than 1 mm, distal margin without tumor, and completeness of TME. Surgical resections occurred in 240 patients randomized to lap and 222 with open resection. Successful resection occurred in 81.7% of lap cases (95% CI, 76.8%–86.6%) and 86.9% of open resection cases (95% CI, 82.5%–91.4%) and did not support noninferiority (difference, −5.3%; 1-sided 95% CI, −10.8% to ∞; P for noninferiority = .41). Conversion to open resection occurred in 11.3% of patients. Patients underwent LAR (76.7%) or APR (23.3%). Operative time was significantly longer for lap resections (mean, 266.2 vs 220.6 minutes; mean difference, 45.5 minutes; 95% CI, 27.7–63.4; P < .001) while length of stay (7.3 vs 7.0 days; mean difference, 0.3 days; 95% CI, −0.6–1.1), readmission within 30 days (3.3% vs 4.1%; difference, −0.7%; 95% CI, −4.2% to 2.7%), and severe complications (22.5% vs 22.1%; difference, 0.4%; 95% CI, −4.2% to 2.7%) did not significantly differ. The TME was complete (77%) and nearly complete (16.5%) in 93.5% of the cases. Negative CRM was observed in 90% of the overall group (87.9% laparoscopic resection and 92.3% open resection; P = .11) while distal margin result was negative in more than 98% of patients irrespective of type of surgery (P = .91). Thus, the use of lap resection compared with open resection failed to meet the criterion for noninferiority for pathologic outcomes and do not support the use of lap resection in these patients.


This study sought to compare the outcomes of patients with rectal cancer undergoing conventional APR versus cylindrical APR (cyAPR). Between January 2008 and December 2010, sixty-seven patients with T3-T4 low rectal cancer were identified and randomized (conventional n = 32, cylindrical n = 35). Those who received cyAPR had less operative time for the perineal portion (P < .001), larger perineal defect (P < .001), less intraoperative blood loss (P = .001), larger total cross-sectional tissue area (P < .001), similar total operative time (P = .096), and more incidence of perineal pain (P < .001). The local recurrence of the cyAPR group was statistically improved (P = .048). The authors concluded that cyAPR in the prone jackknife position has the potential to reduce the risk of LR without increased complications when compared with conventional APR in the lithotomy position for the treatment of low rectal cancer.


NSABP R-04 was designed to determine whether the oral FP capecitabine (cape) could be substituted for continuous infusion (CIVI) 5-FU in the curative setting of stage II/III rectal cancer during neoadjuvant radiation therapy and whether the addition of oxaliplatin could further enhance the activity of fluoropyrimidine-sensitized radiation. This was a 2 × 2 trial design: CIVI 5-FU or oral cape with or without oxaliplatin. The primary endpoint was local-regional tumor control. Among 1608 randomized patients there were no statistically significant differences between regimens using 5-FU versus cape in 3-year local-regional tumor event rates (11.2% vs 11.8%), 5-year DFS (66.4% vs 67.7%), or 5-year OS (79.9% vs 80.8%); or for oxaliplatin versus no oxaliplatin for the three endpoints of local-regional events, DFS, and OS (11.2% vs 12.1%, 69.2% vs 64.2%, and 81.3% vs 79.0%). The addition of
oxaliplatin was associated with statistically significantly more overall and grade 3 to 4 diarrhea ($P<.0001$). Three-year rates of local-regional recurrence among patients who underwent R0 resection ranged from 3.1% to 5.1% depending on the study arm. This study established capecitabine as a standard of care in the pre-operative rectal setting while the addition of oxaliplatin failed to improve the local-regional failure rate, DFS, or OS for any patient risk group but did add toxicity.


This study aimed to determine the impact of adjuvant chemotherapy for patients with rectal cancer, especially when used after preoperative CRT. The RCT was designed to compare the efficacy and safety of adjuvant fluorouracil and leucovorin with that of FOLFOX in patients with locally advanced rectal cancer after preoperative CRT. Patients with postoperative pathologic stage II (ypT3-4N0) or III (ypTanyN1-2) rectal cancer after receiving neoadjuvant FP-based CRT and TME were randomized to receive 4 months of adjuvant chemotherapy with either fluorouracil and leucovorin or FOLFOX. The primary endpoint was 3-year DFS, analyzed by intention to treat. Three hundred twenty-one patients were randomly assigned to fluorouracil and leucovorin ($n=161$) or FOLFOX ($n=160$). Most all patients (141 [95%] of 149 patients in the fluorouracil plus leucovorin group and 141 [97%] of 146 in the FOLFOX group) completed all planned cycles of adjuvant treatment. Three-year DFS was 71.6% (95% CI 64.6–78.6) in the FOLFOX group and 62.9% (55.4–70.4) in the fluorouracil plus leucovorin group (hazard ratio 0.657, 95% CI 0.434–0.994; $P=0.047$). Any grade neutropenia, thrombocytopenia, fatigue, nausea, and sensory neuropathy were significantly more common in the FOLFOX group; however, however, there were no significant differences in these grade 3 or 4 toxicities. In this patient population, the authors demonstrated that adjuvant FOLFOX improved DFS compared with fluorouracil plus leucovorin after preoperative CRT and TME.

REFERENCES


51. Francois Y, Nemoz CJ, Baulieux J, et al. Influence of the interval between preoperative radiation therapy and surgery on downstaging and on the rate of


