Robotic surgery in colorectal cancer: the way forward or a passing fad

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Abstract: Introduced mainly to overcome the technical limitations of laparoscopy, robotic colorectal surgery (CRS) has been touted to provide superior optics, ergonomics, and surgeon autonomy. This technological advancement is nonetheless associated with certain drawbacks, mainly involving its cost and the lack of unequivocal benefit over conventional laparoscopy. In this era of evidence-based medicine, robotic CRS remains predominantly a subject of individual institution case series, retrospective studies, matched comparisons at best, and repeated reviews of the above literature. This article provides a critique of the more contemporary data regarding the use of robotics in colorectal cancer surgery and the controversies surrounding the literature.

Keywords: Surgery; cancer; colorectal; laparoscopy; robot

In this era of evidence-based medicine, robotic CRS remains predominantly a subject of individual institution case series, retrospective studies, matched comparisons at best, and repeated reviews of the above literature. The quality of these publications have previously been criticized (3). However, despite the cost and equivocal evidence, the use of robotics in CRS continues to increase.

This article provides a critique of the more contemporary data regarding the use of robotics in colorectal cancer surgery and the controversies surrounding the literature.

Why the best-quality evidence was not the best evidence

Being a form of assisted-laparoscopy, robotics would expectedly share the short-term benefits of MIS. Outcomes like intraoperative blood loss, time to resolution of ileus, postoperative analgesia requirements and length of stay...
presented an analysis that would be the more appropriate yardstick to compare robotics against.

In one of the most recent meta-analysis of five randomized controlled trials (RCT) on MIS for rectal cancer, the authors showed a moderate quality of evidence that robotics was associated with a lower conversion rate (RR 0.58; 95% CI: 0.35–0.97, P=0.04) and longer operating time (mean difference 38.43 minutes, 95% CI: 31.84–45.01, P<0.00001) compared to laparoscopic surgery (4). The reviewers failed to mention, however, that one of the included studies had deviated from its randomization protocol (5). In the smaller studies by Baik and Jiménez Rodríguez, robotic assistance showed no benefit over laparoscopy, although their limited sample sizes (36 and 56, respectively) were arguably not adequately powered to demonstrate statistical significance (6,7). Indeed, there was either no power calculation, or the basis for the stipulated sample size was not detailed by the authors of these studies. The largest and most well-designed study remains the Robotic Versus Laparoscopic Resection for Rectal Cancer (ROLARR) trial (8).

The much anticipated results of the ROLARR trial came as a surprise to many, and a disappointment to proponents of robotic CRS. While the study design was sound, the unexpected improvements in laparoscopic rectal surgery over the accrual period resulted in a flawed sample size calculation. Based on the 12.2% conversion rate in the laparoscopic arm, at least 700 subjects (not yet accounting for attrition) would have been required to show a 50% reduction in this primary outcome of the study, instead of the 466 patients who actually completed the trial. In addition, the authors used confidence interval calculations to hypothesize that a sample of 400 patients would have been sufficient to analyze differences in the secondary outcomes of CRM positivity and 3-year local recurrence—this, unfortunately, was also based on data from the Medical Research Council Conventional versus Laparoscopic-Assisted Surgery in Colorectal Cancer (MRC CLASICC) trial (9). The CRM positivity rate was 16% in the MRC CLASICC, whereas ROLARR reported a 6.3% positivity rate for laparoscopy and 5.1% for robotics. The 3-year data from ROLARR showed no difference in local recurrence, disease-free survival, and overall survival between the two MIS approaches. The discrepancy in surgeon experience was also criticized. While the pre-requisite was at least 30 MIS rectal cancer resections (at least 10 laparoscopic and at least 10 robotic) prior to participating in the study, the median number of laparoscopic and robotic procedures performed by the surgeons was 91.4 (range, 10.0–853.0) and 49.5 (range, 10.3–183.0), respectively. While one may be quick to point out that robotics is supposed to be credited with a shorter learning curve, the actual number of cases required to achieve competency should perhaps be a more realistic reflection of individual surgeon competencies. Indeed, the sensitivity analysis exploring learning effects suggested a potential benefit of robotics when performed by ROLARR surgeons with substantial prior experience, regardless of their background in laparoscopy.

One of the high-volume (180 rectal cancer operations annually, with 79% performed robotically) robotic surgery centers from the ROLARR trial recently published their results separately and demonstrated a lower opioid consumption during robotic surgery (P=0.0001) (10). While this could possibly have been attributable to the significantly lower conversion rate to open surgery, the statistical difference remained even after the cases of conversion were excluded from the analysis (P=0.007). The authors hypothesized that the limited reach of laparoscopic instruments resulted in increased stress, and therefore pain, at the laparoscopic port sites during mesorectal dissection.

In one of the few trials that involved an operator with an equivalent experience in robotic and laparoscopic rectal cancer surgery, Park et al. reported a 7.1% conversion rate with laparoscopy, with no conversions amongst the 133 robotic cases reviewed (P=0.003) (11). While this result was likely attributable to a certain degree of selection bias, the two groups of patients were nonetheless comparable in terms of gender, BMI, tumor location, and the use of preoperative chemoradiotherapy. However, the authors concluded that robotics provided no long-term oncological advantage based on their 5-year survival and local recurrence data (median follow-up 58 months, interquartile range 49–66 months).

What do we expect robotics to be good for?

The narrow confines of the pelvis remain a technical challenge for rectal cancer surgery in male patients. Despite the limitations of their study, Baek et al. presented an interesting finding from their review of anatomical difficulty in patients who had undergone robotic rectal cancer surgery (12). Patients were stratified into three groups based on MRI pelvimetry—easy, moderate, and difficult pelvic anatomy. The authors found no difference between

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the groups in terms of surgical outcomes, leading them to postulate that robotics compensated for the level of surgical difficulty and may be beneficial when operating on patients with a difficult pelvic anatomy.

In obese patients, the bulky mesorectum compounds the problem of restricted access when operating in a narrow pelvis. The added range of motion of robotic instruments and the enhanced ergonomics that they confer would expectedly be beneficial in this group of patients. In a propensity score matched analysis of MIS rectal cancer resections in obese patients (defined as patients with a body mass index BMI ≥30 kg/m²), Panteleimonitis et al. showed that robotic rectal surgery was associated with a shorter LOS (6 vs. 8, P=0.014) and a lower 30-day readmission rate (6.3% vs. 19.7%, P=0.033) (13). There were two (3.3%) conversions in the laparoscopic group, and none in the robotic group (P=0.24). Earlier retrospective studies have demonstrated similar findings. In their comparison of 29 robotic and 27 laparoscopic obese rectal surgery patients, Gorgun et al. showed a shorter LOS (6 vs. 7 days, P=0.02) and a quicker return to bowel function (3 vs. 4 days, P=0.01) (14). The conversion rates were 3.4% and 18.5% in the robotic and laparoscopic groups, respectively (P=0.09). In addition to a shorter LOS (7 vs. P<0.001), Shiomi et al. also showed lesser blood loss (10.5 vs. 34 mL, P=0.002) and lower complication rates (9.6% vs. 30%, P=0.04) in their robotic group (n=52, vs. n=30 laparoscopic patients) (15). The difference in conversion rate was again not statistically significant.

In the ROLARR subgroup analysis, the conversion rates for laparoscopy were higher in males (16.0%), obese patients (27.8%) and patients undergoing a low anterior resection (13.3%). The corresponding rates in the robotic arm were 8.7%, 18.9% and 7.2%, respectively (8). While there were insufficient patients to provide statistically meaningful comparisons, these figures may nonetheless remain clinically relevant. Similarly, in their study of high-risk patients (defined as BMI ≥30 kg/m², male gender, preoperative chemoradiotherapy, tumor <8 cm from anal verge, or previous open abdominal surgery), Ahmed et al. showed that robotic rectal cancer surgery was associated with reduced blood loss, lower conversion rates, shorter operative time and a shorter length of hospitalization compared to laparoscopy (16). Based on the greater percentage of anterior resections in the robotic group, the authors also concluded that robotics allowed for a greater chance of sphincter preservation and avoidance of a permanent stoma.

Another purported benefit of robotics has been the preservation of neurological function by allowing more precise dissection. A prospective cohort study conducted in South Korea between June 2009 and November 2009 analyzed the urogenital function after robot-assisted and laparoscopic total mesorectal excision (TME) (17). The authors reported an earlier recovery of normal urinary voiding in the robotic group, with the IPSS recovering in 3 months compared to 6 months in the laparoscopic group. The change from preoperative values in mean voiding volume based on urodynamic study was also significantly less in the robotic group at 3 and 6 months after surgery (P=0.007 and P=0.049, respectively). While the IIEF scores were not significantly different between the two groups, there was a faster recovery time associated with robotic TME (6 vs. 12 months after laparoscopy). In a similar comparison by Park et al., thirty-two male patients who underwent robotic TME between February 2009 and December 2010 were matched with a group selected from 51 men who underwent laparoscopic TME (18). The robotic group reported an earlier restoration of erectile function, while the mean IPSS scores did not differ from the laparoscopic group. Postoperative bladder function was analyzed in 351 (75.3%) of the 466 ROLARR subjects, and sexual function assessment was complete in an even smaller number (181 men and 54 women) of patients. There was no significant difference between laparoscopy and robotics. However, another randomized trial of patients in China who underwent laparoscopic or robotic rectal cancer surgery between November 2010 and September 2013 reported results to the contrary (19). Wang et al. evaluated the urinary and sexual function in 137 (of 336) male patients. While the authors did not describe their sample size calculation, they managed to show that the total International Prostate Symptom Score (IPSS) was significantly increased after surgery in patients who underwent laparoscopic surgery (9.66 vs. 4.12, P=0.031), while there was no significant difference in the robotic group (6.79 vs. 4.04, P=0.068). The incidence of sexual dysfunction was also significantly lower (P=0.033), with total International Index of Erectile Function (IIEF) scores significantly higher in the robotic group (46.2 vs. 40.1, P=0.043).

Should robotics be used for colon cancer surgery?

The evidence for robotic colectomy is even less compelling (20).
Overall, the most consistent findings were that robotic colectomies tend to be associated with longer operative times and higher cost. Studies analyzing left-sided colectomies have essentially failed to show a significant benefit in the use of robotics (21,22).

In one of the few prospectively conducted trials on right-sided colectomies, Park et al. analyzed 70 patients who were randomized to either robotic or laparoscopic surgery for right-sided colon cancer (23). Their study has remained the only RCT in the repeated meta-analyses on this topic. Powered to show a 1-day difference in LOS using a 7-day hospital stay as the baseline, the study failed to show a benefit in robotics (LOS in robotic group 7.9 days vs. 8.3 in laparoscopic group, P=0.130). In keeping with most studies comparing robotics against laparoscopy, the operator was an expert laparoscopic surgeon, whereas the operating team had undertaken only 5 robotic colectomies (and a total of 30 robotic procedures) prior to embarking on the trial. While not objectively measured, the authors did comment that lymphadenectomy around major vessels was easier with robot assistance. This subjective benefit has also been expressed by other authors, but to date remains an anecdotal advantage (24,25).

Along with the RCT by Park et al., many other reports on robotic colectomy have also been criticized for not standardizing the method of anastomosis (i.e., intra- or extracorporeal) in their comparison with laparoscopy (21,23,26,27). A case in point is the study by Trastulli et al. (24). The benefits of robotics in this retrospective analysis were attributed primarily to the intracorporeal nature of the anastomosis in robotic colectomy, instead of a true difference between robotics and laparoscopy. In an attempt to exclude this confounder, Solaini et al. conducted one of the largest retrospective studies analyzing only MIS right colectomies that involved an intracorporeal anastomosis (28). This unmatched cohort had significantly more patients in the robotic arm (n=305, vs. laparoscopic n=84), although the authors reported no significant differences between the groups in terms of baseline characteristics. The robotic group was associated with a significantly higher number of lymph nodes harvested (22 vs. 10, P=0.028) and a lower 90-day readmission rate (0.3% vs. 3.6%, P=0.033), although it remains questionable if these results translate into clinical significance—the minimum number of lymph nodes harvested was 15, above the obligatory standard of 12; the absolute number of readmissions was 1 in the robotic group and 3 in the laparoscopic group. Perhaps more importantly, this study illustrates how robotics serves as an enabling tool that allows surgeons to perform intracorporeal anastomosis with greater ease. Other studies have also reported a higher lymph node yield with robotic right colectomies, albeit after statistical matching or multivariate analysis (25,29).

In one of the most recent clinical database studies based on the National Surgical Quality Improvement Project (NSQIP) data between 2013 and 2015, Kulaylat et al. showed that elective robotic colectomies were associated with a lower conversion rate (6.0% vs. 11.5%, P<0.001) and a shorter LOS (4.6 vs. 5.2 days, P<0.001) when compared to laparoscopic colectomies after propensity score matching (30). However, only 55.5% to 59.2% of the cases in this analysis involved colorectal malignancies. Multiple similar reviews have been derived from the NSQIP and National Inpatient Sample (NIS) datasets, and their findings have remained relatively consistent with the above (31-38). There will undoubtedly continue to be publications extending the time period of analysis as the database expands. However, it would be prudent to interpret these results in the context of the known limitations of propensity score matching, multivariable analyses and database research (39,40).

Another publication that analysed the combined data of left- and right-sided colonic cancer resections showed that patients who underwent robotic surgery reported a shorter time to diet intake, passage of flatus, and defecation (41). Robotic surgery was also associated with lower estimated blood loss, longer proximal margin, and a shorter hospital stay, albeit at the expense of longer surgery time. While the results suggest potential advantages of robotics in colon cancer surgery, they need to be interpreted with some degree of circumspection—out of the six studies analysed, the risk of bias in the included RCT was high, and the quality of the cohort studies was poor.

The way forward for robotics in colorectal cancer surgery

In order for robotic CRS to avoid being a passing fad, we see the need for development in two areas—more robust scientific evidence and an improvement in cost-benefit.

There are currently several randomized studies listed on ClinicalTrials.gov (42-44). In addition, the role of robotic systems in more technically demanding procedures like multivisceral resection for locally-advanced pelvic tumors, pelvic lymph node dissection, transanal natural-orifice surgeries, and hemicolecotomies with complete mesocolic excision-central vascular ligation should be
investigated. Future research should aim to provide evidence substantiating the claim that robotics provides superior ergonomics. While no studies have reported results to the contrary, surgeon ergonomics remains an entity that is subjective and contentious to compare. Innovative methods of measurement should therefore be devised to provide objective assessments of (I) the stability and orientation of the endoscopic view, (II) the reduced dependence on bedside assistance, (III) the resultant improvement in efficiency of surgical retraction and dissection, and (IV) the overall reduction in stress and fatigue experienced by the operator. Similarly, more emphasis should be placed on evaluating functional outcomes in order to examine the hypothesis that the precision of the surgical robot results in superior nerve preservation. Given the significant technological advancements in recent years, comparisons should perhaps be made between the different generations of robotic systems. For example, the multiquadrant capabilities and extended features of the da Vinci Xi would potentially address the issues of prolonged docking and operating times of the earlier da Vinci models (45). Further publication of retrospective reviews and registry data-mining should be curtailed until more contemporary studies are available. Having already established the safety and feasibility of robotic CRS, journals should be more discerning against submissions that report small case series of “early experience” and “initial results”.

While the current robotic surgical market is essentially a monopoly, numerous competitors have been vying to provide alternatives. These include TransEnterix (Morrisville, NC, USA), Cambridge Medical Robotics (UK), Meere Company (South Korea), Verb Surgical, Medtronic, Vecna Technologies, Titan Medical (Toronto, ON, Canada), and Virtual Incision (Pleasanton, CA, USA). One would be naive to assume there will be a significant reduction in cost, but it might be reasonable to expect the price of robotics to be moderated to a certain extent. Coupled with better evidence to support the benefits of robotic technology, the cost-benefit might become more compelling for healthcare systems.

Acknowledgments
None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Cite this article as: Ngu JC, Kim SH. Robotic surgery in colorectal cancer: the way forward or a passing fad. J Gastrointest Oncol 2019;10(6):1222-1228. doi: 10.21037/jgo.2019.04.01