Editorial

Minimally invasive proctectomy for locally advanced rectal cancer: is less always more?

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Comment on: Sujatha-Bhaskar S, Jafari MD, Gahagan JV, *et al.* Defining the Role of Minimally Invasive Proctectomy for Locally Advanced Rectal Adenocarcinoma. Ann Surg 2017;266:574-81.

Received: 13 December 2017; Accepted: 30 December 2017; Published: 15 January 2018.

doi: 10.21037/ales.2017.12.09

View this article at: http://dx.doi.org/10.21037/ales.2017.12.09

Colorectal cancer (CRC) is the 3rd most common cancer worldwide, with rectal cancer accounting for approximately 1/3 of CRC cases (1). Although there has been increasing interest in the primary treatment of rectal cancer with chemoradiotherapy in patients who experience complete clinical response, surgical management remains the gold standard treatment for curable cases and has seen significant advances in the past 4 decades (2). Total mesorectal excision (TME) which was first described by Prof. Bill Heald in 1982, saw a remarkable improvement in rates of local control for rectal cancer and paved the way for future rectal surgery (3). Advances in neoadjuvant therapies have seen a further reduction in local recurrence rates, particularly for more locally advanced tumours. With improving oncological outcomes there has been a constant drive to improve surgical technique, allowing surgeons to reach these outcomes whilst minimising the physiological impact on patients perioperatively, and allowing for greater long-term function. Rates of sphincter preserving surgery and the avoidance of a permanent colostomy have improved with improvements in surgical technique and advances in device technology. Minimally invasive surgical techniques have also developed significantly since the first laparoscopic colorectal resections in the early 1990s.

The recognised benefits of laparoscopic surgery which include; reduced wound-related complications, reduced post-operative pain, earlier return of bowel function, earlier commencement of adjuvant chemotherapy when required and earlier discharge from hospital have been the driving force for the development of the technique and the technology which has made it available (4,5). In larger academic centres, laparoscopic surgery is now progressing to the next stage with the introduction of robotic surgery, and in the field of colorectal surgery, transanal minimally invasive techniques. Given the preference for minimally invasive techniques for rectal cancer surgery in many centres worldwide, the question of oncological outcomes and their equivalence to open rectal resections remains an area of controversy. Unfortunately, many of the studies published to date designed to answer this question—such as that produced by Sujatha-Bhaskar *et al.* have produced conflicting results (5-9).

In the current body of evidence there are five randomised control trials (RCTs) which have aimed to answer the above question and are considered the most influential (5-9). Of these 5 studies, the results of 3 support laparoscopic surgery as being oncologically equivalent to open rectal resection whilst 2 non-inferiority studies failed to show non-inferiority. The Medical Research Council CLASICC trial was the first trial to assess the comparative oncological efficacy of laparoscopic surgery and open colorectal surgery (5). Although it did not specifically investigate rectal resection, 381/794 patients with rectal cancer underwent randomisation to open and laparoscopic resection whilst the remaining 413 patients had colonic resections. Long term results of this study found no difference in long term overall survival and disease-free survival when comparing laparoscopic and open rectal

resection groups. These finding were despite initial short-term results showing a non-statistically significant increase in circumferential resection margin (CRM) positivity for laparoscopic anterior resection specimens (12%) compared to open anterior resection specimens (6%). The CLASICC trial has also been criticised for its high conversion rate of 34% which raised some initial concerns for the applicability of laparoscopic rectal resection (8). The high conversion rate seen in this trial has been attributed to a relatively limited level of technical experience by those surgeons performing the laparoscopic rectal resections. This limitation was recognised by investigators who subsequently conducted similar RCTs (6-9). In these following studies, surgeons were required to submit video recording of laparoscopic rectal resections, and in some cases the pathology specimens were also assessed for completeness of TME. This, along with improving equipment, saw recorded conversion rates decrease to as low as 1% as seen in the COREAN trial (6).

Following the results of the CLASSIC trial, similar trials such as the COREAN and COLOR II trials also found that laparoscopic surgery was non-inferior to open surgery for rectal cancer (6,7). The two trials differed in a number of respects with regard to eligible patients and the number of centres involved. The COREAN trial aimed to compare outcomes for patients with more locally advanced tumours who underwent neoadjuvant and adjuvant therapy (6). The patients in this study also had tumours only in the mid and low rectum. Patients enrolled in the COLOR II trial generally had less locally advanced tumours, a lower proportion of patients had neoadjuvant therapy (30%) and the primary tumour could be located anywhere within 15 cm from the anal verge (only 29% located in the lower rectum) (7). In both the COREAN and COLOR II trials, T4 tumours were excluded and in the COLOR II trial T3 tumours within 2 mm from the endopelvic fascia were excluded, meaning that not all rectal cancer patients were represented. Not only did both these studies prove oncological non-inferiority, both also confirmed the short term benefits associated with laparoscopic surgery such as earlier return of gut function, less pain and earlier discharge from hospital. Although the overall results of both these studies supported laparoscopic surgery, some specific results and patient-related factors require consideration. The COREAN trial for example had a patient population with a mean body mass index (BMI) of 24. Such a low BMI is something seen far less in western centres and may have led to the low conversion rate see in the trial. Also in the COREAN trial, although the positive CRM rate was low at 3%, the rate of complete mesorectal excision was unexpectedly low at 73%. The high rate of positive CRM in low rectal tumours (22% for open resections) and the high permanent stoma rates seen in the COLOR II trial have also raised questions from other experts in the field.

The American ACOSOG Z6051 trial and the Australia and New Zealand ALaCaRT trial are two RCTs that failed to show non-inferiority of laparoscopic rectal resection (8,9). Both trials, which placed emphasis on high quality surgery and quality assurance of pathological specimens, returned results that were not expected by their lead investigators. It was identified by the authors of the ALaCaRT trial that although they had insufficient numbers to allow for subgroup analysis, their results indicated that laparoscopic rectal resection may not be as successful as open surgery for larger tumours, T3 tumours, patients with high BMIs and patients who have had neoadjuvant therapy. These trials also utilised a hybrid technique for open resection whereby mobilisation of the colon down to the peritoneal reflection was performed laparoscopically, followed by a conventional open dissection of the rectum. This hybrid technique resulted in a more similar post-operative course for laparoscopic and open procedures with only length of hospital stay found to be statistically different in the ALaCaRT laparoscopic group. Due to the findings of an inferior oncological outcome and limited short-term post-operative benefit of laparoscopic surgery, the debate regarding the equivalence of laparoscopic rectal resection is still ongoing.

The recent retrospective review performed by Sujatha-Bhaskar *et al.* attempts to further define the role of minimally invasive proctectomy for locally advanced CRC (3). The study has used the American National Cancer Database (NCDB) to identify patients with locally advanced, non-metastatic rectal cancer based on their treatment with neoadjuvant and subsequent adjuvant therapy. Interrogation of such a large database has allowed the authors to identify a large number of eligible patients who have undergone either open, laparoscopic or robotic rectal cancer resections from a variety of American centres. All eligible patients' records were subsequently investigated to identify basic demographic information, comorbidity data, primary tumour pathology and oncological adequacy of resected specimens. The results indicated that significantly higher R0 resection rate for laparoscopic and robotic resection and higher positive CRM rate seen in open resections (7.72% compared to 4.87% for laparoscopic resections). Not

surprisingly given the rates for R0 resection, survival rate estimates demonstrated a trend toward superior survival for laparoscopic and robotic surgery compared to open surgery. Conversion rates for laparoscopic approach were 14% whilst the conversion rate for robotic approach was only 7%, and it was found that converted cases had a higher rate of positive CRM of 10.3%. Although conversion to open would suggest a high level of technical difficulty associated with the case, it may indicate that surgeons need to give greater consideration to using an open approach if a case appears unlikely to be successful laparoscopically.

Although the results of the study indicate the superiority of laparoscopic and robotic rectal resection over an open approach, the authors very openly recognise an underlying bias in the data which has likely led to such conclusions. Laparoscopic and robotic resections were almost entirely performed by surgeons working in high volume centres, where the operating surgeons would be far more technically experienced in rectal dissection. In other words, the results do not necessarily indicate the superiority of a technique but rather indicate that experienced colorectal surgeons will have lower rates of involved CRMs when compared with lower volume non-specialist surgeons performing open rectal surgery. Interestingly, although the study included results from less experienced surgeons operating in lower volume centres, the overall rates of positive CRM were comparatively low to those observed in the COLOR II (10% for open and laparoscopic) and the ASOCOG Z6051 (7.7% for open and 12.1% for laparoscopic) trials. This however may be due to associated variables such as number of high rectal cancers treated and percentage of patients undergoing neoadjuvant treatment. The high rates of partial proctectomy (56% for open, 63% for laparoscopic and 62% for robotic), would suggest that a high number of patients involved in this study had high rectal tumours.

Although the retrospective trial aimed to further define the role of minimally invasive surgery for proctectomy in locally advanced rectal cancers, it has further highlighted the greater success of trained colorectal surgeons achieving better oncological results. It has essentially shown that laparoscopic and robotic proctectomy, when performed by trained colorectal surgeons, are superior to open proctectomy when performed by the general surgical community. This would indicate that where logistically possible, patients should be referred to high volume centres with trained colorectal surgeons for their rectal cancer surgery, rather than being treated by a general surgeon.

Based on a review of current literature, the question regarding the equivalence or otherwise of oncological outcomes for laparoscopic proctectomy compared to open proctectomy remains unanswered. Given the lack of strong evidence supporting either technique, it is unlikely that there has been a significant shift in treatment regimens by investigators involved in studies which found laparoscopic proctectomy is inferior to open proctectomy, and that a hybrid operation would offer superior oncological outcomes with acceptable short-term post-operative results (i.e., pain and return of gut function). The available studies are heterogenous for geographic location, patient population variables (e.g., BMI, tumour stage and neoadjuvant therapy) and level of surgical experience. This heterogeneity has given rise to a range of results which may reflect more the population being treated and by whom they are being treated, rather than by which technique the have been treated. It is possible that laparoscopic surgery is superior to open rectal resection, however this may only be for certain patient populations, based on BMI and tumour pathology. Hence it may be more effective to investigate which patients are best suited for individual techniques so that treatment regimes can be tailored for individual patients.

Although it would appear more research is required to define if laparoscopic proctectomy is non-inferior to open, the academic surgical community has already continued past laparoscopic surgery and has moved onto more advanced minimally invasive techniques. Robotic surgery and Transanal TME (TaTME) are two minimally invasive techniques that have been created in order to alleviate difficulties and shortcomings associated with laparoscopic TME dissection. Although laparoscopy allows for good visualisation within the pelvis, working in line with rigid instruments can make working in a narrow pelvis of an obese patient with a narrow pelvis and locally advanced pathology incredibly challenging. Robotic surgery allows for a 3-dimensional view, removes surgical tremor, offers greater dexterity of working instruments and reduces surgeon fatigue (10). These factors have been reflected by lower conversion rates. Transal TME allows for a retrograde dissection of the rectum, with dissection commencing below the tumour and progressing toward the peritoneal reflection (11). This approach thus aims to remove the difficulty associated with the narrow android pelvis where a low anterograde dissection to get below a tumour is difficult. The ROLARR and COLOR III are two RCTS currently in progress which respectively compare robotic TME and TaTME with laparoscopic TME. It will be interesting to see whether robotic TME and TaTME are

compared to open TME to assess oncological equivalence if they are shown to be superior to laparoscopic TME.

With the increasing availability of newer surgical devices, technology and techniques driving towards a more minimally invasive approach, surgeons need to remain mindful of the need to place patient outcomes first. Newer approaches are not always better and the current body of evidence relating to minimally invasive techniques to manage rectal cancers needs to be reviewed with some scepticism. It appears that each patient and their pathology need to be viewed and managed on their own merits. Until better evidence is available, it appears that in the age of less is more, open surgery may still have a role in managing some rectal cancers.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Annals of Laparoscopic and Endoscopic Surgery*. The article did not undergo external peer review.

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/ales.2017.12.09). 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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doi: 10.21037/ales.2017.12.09
Cite this article as: Croese A, Nabi H. Minimally invasive proctectomy for locally advanced rectal cancer: is less always more? Ann Laparosc Endosc Surg 2018;3:4.