



# Current status of minimally invasive surgery in colorectum

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Colorectal cancer (CRC) is the third most common cancers in men and second most common in women with incidence rates of 15–21 per 10,000 worldwide (1). Surgery is the only curative therapy for CRC, with the advancement in surgical technology and understanding the concepts of anatomy and pathology impelled to increase in survival. Technology and experience had transformed the field of colorectal surgery in diverse aspect, as there are no standardization of surgical technique and minimally invasive surgery (MIS) still it is in evolving process, whether to adopt with the new perspective depends on the experience and available evidence which this article brings forth the current practice of MIS in colorectal surgery.

## Present state of MIS in colon surgery

Laparoscopic colorectal surgery follows the same oncological principles as open surgery with adequate lymphadenectomy, high ligation of vessel, adequate bowel margins. Since first reported laparoscopic colectomy by Jacob it has become standard surgical procedure in majority of centres. During initial period of MIS there were concern of port site metastasis and long term outcome in laparoscopic colon surgery, but last 2 decades have shown level one evidence suggesting that laparoscopy has good short and long term benefits as compared to open surgery. There are randomised control trials (RCTs) (1-9) (Table 1) and meta-analysis (10) suggesting the laparoscopy has better outcome compared to open colectomy showing benefits in terms of decreased intraoperative complications, decreased transfusions, early recovery of bowel function, decreased analgesic, short hospital stay, smaller incision, CRM margins and cost. However, laparoscopy did not jeopardise

the oncological outcome (2-6).

In large data base of over 3,00,000 cases from ACS NSQIP (national surgical quality improvement programme, 2006–2013) the number of laparoscopic colorectal cases performed are 36–49% (11). The context of the studies and the practical applicability differs with the experience of the surgeon, high volume centres and the standardised technique practised which finally gives better outcomes.

## Concepts and controversies of complete mesocolic excision (CME)

In rectal cancer adoption of total mesocolic excision principles of surgery has reduced the local recurrence (LR) rates and improved the survival. The anatomical and embryological planes continue from rectosigmoid, descending colon, and run posteriorly behind the pancreas to include duodenum, cecum, ascending colon and the mesenteric root. Removal of tumour along the mesocolic plane increases survival benefits, concept of CME raised from this anatomical basis. The 10-year outcomes of CLASSIC trial (6) concluded in subgroup analysis that laparoscopic right hemicolectomy has increased propensity for LR than left hemicolectomy. Whether the long term outcomes of surgery based on the CME principles results could transform in better outcome is the matter of debate.

CME involves three principles: (I) removal of central envelop in mesocolic plane; (II) high vascular tie; (III) sufficient length of bowel both proximally and distally (12). Proponents of CME put forward that there are high number of lymph node harvested and eradicating the lymphatic's better achieves local control of cancer, high lymph

Table 1 RCT of MIS in colon cancer

Trial	Period	No. of patients	Lap/open	Follow up	Primary outcome	Short term outcomes (laparoscopy vs. open)	Long term outcomes (laparoscopy vs. open)
COST (2,3) [2004, 2007]	1994–2001	872	435/428	4.4 y	Time of tumour recurrence	Laparoscopy had faster recovery, short hospital stay, decreased parenteral and analgesic use, with similar 30 day mortality, morbidity, readmissions, reoperations compared to open	3 y RR similar (lap 16% vs. 18% open), RR at wound sites similar (1% vs. 1%), OS is similar (lap 86% vs. 85% open)
CLASSIC (4,5) [2007]	1996–2002	794 (52% colon)	2:1 ratio	62 m	3 y OS/DFS/LR	No difference in OS (78.3% vs. 82.7%); DFS (89% vs. 77%), RR. Conversion rates 16–38%	Conversion to open has worse OS
CLASSIC (6) [2013]	1996–2002	794	526/268	10 y	SR/RR		Laparoscopy has similar long term outcomes. Right colon cancers has increased LR than left colon (14% vs. 5%)
COLOR 1 (7) [2005]	1997–2003	1,248	536/546	3 y	3 y cancer free survival	Laparoscopy has less blood loss, early bowel function, less analgesic requirement, short stay. No difference in number of lymph node retrieval, mortality and morbidity. Conversion rates 17%	
COLOR (8) [2009]	1997–2003	1,076	627/621	3 y	3 y DFS		No difference in DFS (76% vs. 74%), OS (84% vs. 81%)
ALCCaS (9)	1998–2005	601	294/298		Operative, perioperative and HPE details	Laparoscopy had short stay, early recovery of GIT. Significant haemorrhage in laparoscopy group (10% vs. 3%). Conversion rates 14%. Laparoscopy showed shorter distal margin in right hemicolectomy	

Lap, laparoscopy; open, open surgery; DFS, disease free survival; OS, overall survival; LR, local recurrence; RR, recurrence rates; y, years; m, months; GIT, gastrointestinal tract; HPE, histopathological examination; COST, Clinical Outcomes of Surgical Therapy Study Group; CLASSIC, Conventional versus Laparoscopic-Assisted Surgery in Colorectal Cancer; COLOR I, Colon Cancer Laparoscopic or Open Resection; ALCCaS, Australasian Randomized Clinical Study Comparing Laparoscopic and Conventional Open Surgical Treatments for Colon Cancer Trial.

node ratio, identify the skip metastasis, stage migration, identification of micrometastasis, high quality of surgical specimen, and sufficient length of bowel. Opponents argued that the theoretical benefit of removing mesocolic lymph node is minimal as there are other confounding factors for the survival, there is no difference in survival if more than 12 lymph nodes are removed, incidence of D3 lymph node involvement is less and CME leads to over treatment of disease and there are no RCT to support the evidence. There are scepticisms regarding implementation of CME technique in terms of feasibility, and safety in clinical practice.

CME involves sharp dissection under embryological planes between visceral and parietal fascia which was first described by Hohenberger *et al.* (13), he achieved improvement in 5-year survival from 82% to 89% and reduction in 5-year LR from 6.5% to 3.6%. West *et al.* (14) demonstrated 15% survival advantage, increase plane of resection in CME specimens (92% *vs.* 40%) and increase LN retrieval (30 *vs.* 18). The study concluded that CME produced good quality specimens, this was further validated by number of studies (15-22). Storli *et al.* (23) supported the CME with high 3-year SR 88% and increase in DFS (82% *vs.* 75%) compared to non CME patients. Bertelsen *et al.* (24) in a population based study demonstrated that CME has a predictor of better survival with 4-year SR (85% *vs.* 75%) and low RR (11% *vs.* 16%). Kanemitsu *et al.* study concluded that CME produced better long term survival in right colon cancers (25). Laparoscopic CME offers the similar oncological outcome with advantages of MIS (Table 2). JCOG 0404 (15) is the first RCT comparing laparoscopy verses open D3 dissection, this study concluded that laparoscopy has better short term safety and clinical benefits.

### Current role of MIS in rectum

Laparoscopic techniques has gained promising role in rectal surgery as it provides precise pelvic dissection, better identification of pelvic structure in narrow pelvis, improved magnification and visual angles. Sphincter preserving surgery has been recent trend made achievable with adequate pelvic dissection and adequate distal margins feasible by endostapling. Laparoscopic surgery has technical advantage in male pelvis, morbid obese and in prior chemoradiotherapy and bulky distal tumours.

Meta-analysis and RCT comparing laparoscopy verses open in rectal cancers have shown the feasibility and safety and better short term advantages of laparoscopic

surgery in rectal cancers (4-6,26-30). The difference in the operating time and conversion depends on the experience of the surgeon as COREAN, COLOR, ACOSOG Z6051, ALACaRT trials recorded 1%, 16%, 11%, 9% conversion rates respectively.

The CLASSIC trial (4-6) which included 48% rectal cancer cases concluded the there is no difference in OS (lap 78% *vs.* 82% open), DFS (lap 89% *vs.* 77% open), LR (lap 9% *vs.* 10% open) in 10-year follow up. This study analysis raised concern about a potentially higher positive CRM (laparoscopy 12% *vs.* 6% open,  $P < 0.14$ ) in laparoscopic anterior resection (LAR) group but is not significant. In APR the CRM positivity is higher in laparoscopy (16% *vs.* 14%) but did not reach statistical significance and there is no survival difference in 5-year follow up. There is no difference in mortality and morbidity between laparoscopic and open rectal surgery. Laparoscopy has shorter stay than open in rectal surgery. The COREAN trial (28) observed no difference between CRM, macroscopic quality of the total mesorectal excision (TME), number of harvested lymph nodes or perioperative morbidity between the two groups. COLOR 2 trial included 29% low rectal cancers, the CRM positivity in laparoscopy 9% *vs.* 22% in open and LR 3% in laparoscopy *vs.* 12% in open which was less compared to CLASSIC trial which showed more CRM positivity in laparoscopy (16%), with high LR of 9% in lap *vs.* 10% in open. CLASSIC trial (4-6) had 16% CRM positive after laparoscopic surgery (AR group 12% *vs.* 9%). Higher CRM positivity in COLOR II (26,27) trial is due to the fact that margin involvement is taken as within 2 mm from the lateral surface of the mesorectum, whereas the COREAN (28) study used a 1-mm margin. COREAN (28) study concluded that laparoscopy had better advantages than open in low rectal cancers with low CRM positivity and low recurrence rates. ACOSOG Z6051, ALACaRT multi centric RCT showed non-inferiority of laparoscopic surgery compared with open surgery determined by histopathological evidence (29,30).

After the introduction of TME there is significant reduction in complication of Urinary dysfunction and sexual dysfunction due to preservation of autonomic nerves. With open TME the urinary dysfunction has been 0% to 12% and sexual dysfunction in 10% to 30%. The CLASSIC trial (4-6) reported no difference in bladder dysfunction between laparoscopy and open TME. Hur *et al.* showed that laparoscopy had decrease sexual dysfunction compared to open TME (31).

Table 2 Trials on laparoscopic CME

Trial	Type	No. of patients	Laparoscopy/ open	Stage of disease	Primary end point	Short term outcome (laparoscopy vs. open)	Long term outcome (laparoscopy vs. open)
Japan JCOG 0404 [2014] (15)	RCT	1,057	533/524	Stage 2/3	Efficacy, safety	Lap had less blood loss, short time to pass flatul, decrease use of analgesics, short stay, decreased morbidity	99% underwent D3 dissection in both groups
Korea 2014 (16)	Prospective	168	168 lap	Stage 2/3	Short and long term outcomes	Morbidity: 17%; leak: 5%; no mortality; mean LN retrieval: 27	5 y DFS: 95% in stage 1, 80% in stage 2
Korea 2016 (17)	Prospective	215 right colon	99/116		Short term	Lap retrieved more LN (31 vs. 27), no difference in length of specimen and distal and proximal margin, similar operating time, OS and DFS. Open had more 30 day complication (36% vs. 23%)	
Taiwan 2014 (18)	Prospective	244 right colon	244 lap		5-year follow up RR, OS, DFS	LN retrieved: 34; skip metastasis: 19%; upstaging: 4.5%	5 y cumulative RR: N0, 16%; N1, 21%; N2, 43%; N3, 52%
Denmark 2014 (19)	Prospective 2008–2011	244	244 lap		Quality of specimen	Lap has better quality of specimen, increase mesocolic resection, increase in distance between tumour and artery tie, bowel and artery tie	
Italy 2015 (20)	Retrospective 2008–2013	Right colon	115 lap		Short term and long term	Lap R0: 97%; CRM <1 mm: 2.6%	Better OS in lap in stage II/IIla and b, apical node negative I1C
Taiwan 2006 (21)	Prospective	Recto sigmoid	98 lap	Stage 3	Time of recurrence, 5 y recurrence	Time of recurrence: N0, 56 m; N1, 46 m; N2, 43 m	5 y recurrence: N0, 20%; N1, 23%; N2, 33%; N3, 42%

JCOG, Japan Clinical Oncology Group; Lap, laparoscopy; RR, recurrence rates; OS, overall survival; DFS, disease free survival; CRM, circumferential rectal margins; N, nodal stations; LN, lymph nodes; y, years; m, months.

### Emerging trend of robotic colorectal surgery

Advance imaging and technology has made major leap through with use of robotic in CRCs surgery. With difficult pelvic dissection due to narrow pelvis and anatomical complexity in dissection by laparoscopy, adoption of robotic has added advantage of 3D binocular vision, 7 degrees of motion, high resolution, improved dexterity, tremor reduction, improves pelvic dissection, surgeon controlled camera, stable traction and surgeon comfort.

Since the adoption of robotic in colorectal surgery from 2001 there has been increase studies to validate the outcomes comparing robotic and laparoscopic colorectal surgery. Kang *et al.* (32) concluded that robotic is better in terms of faster recovery, short stay, early recover of bowel, decrease wound infection and decrease complication rate (20% *vs.* 27%) ( $P < 0.034$ ). This has been similar in other studies published by Saklani *et al.* (33) supporting decrease morbidity (16% *vs.* 26%), Park *et al.* reported no difference in complication in robotic compared to laparoscopy (34).

The CLASSIC trial (4-6) showed conversion rates of 16% in laparoscopic rectal surgery. After the adoption of robotic the data showed conversion rates of 0–8% (33–35). In Saklani *et al.*'s series of 74 robotic low rectal cases, the conversion rate is 1% (33). Surgical outcomes in rectal cancer depend on the quality of the specimen, and with the implementation of robotics yielded high quality TME specimen. Kang *et al.* (32) reported low CRM positivity in robotic (4.2% *vs.* 10% lap,  $P < 0.034$ ), Yoo *et al.* 2015 (35) also supported low CME positivity in robotic 9% *vs.* 19%. The drawbacks of robotics are the increase in operating time and cost. Patriti *et al.* demonstrated shorter operating time (165 min) (36).

There are few studies (37,38) to show the long term outcome in robotic surgery, Park *et al.* (37) compared 133 cases of robotic LAR with 5-year follow up showed no difference in OS, DFS, LR. The ROLARR (39) multicentre RCT concluded that there is no difference in conversion rates (8% *vs.* 12%), CRM positivity (5% *vs.* 6%), but robotic surgery showed benefits in males, in low tumour and obese patients.

### Contention in management of transverse colon (T-colon) cancers

T-colon deserves special mention as T-colectomy surgeries are quite challenging. Laparoscopy has better benefits

in T-colon as better visualization of mesentery base, identification of middle colic vessels, better dissection of mesentery from pancreas. T-colon has special anatomical and embryological status and surgery in T-colon is not standardised, because of an embryological fusion of mesenteric fascia, metastatic nodes incidence is 5% in subpyloric and 4% in right gastroepiploic nodal station (40). Most of the randomised trials like CLASSIC, COST, COLOR, ALCCas, have not included T-colon cancer.

Agarwal *et al.* (41) showed that laparoscopy retrieved more LN yield (22 *vs.* 18) and laparoscopy is feasible with conversion of 10% cases, further laparoscopy had decreased stay and similar 5-year OS and DFS, RR. Chong *et al.* published largest series of 1,060 patients comparing outcomes of T-colectomy versus extended colectomy which showed no difference in 5-year DFS/OS (42).

### Distinction of combined endoscopic and laparoscopic surgery (CELS) in colorectal surgery

CELS is a recent development for removal of colonic polyps when endoscopically difficult for excision when polyp is large, broad base, difficult visualization between the folds of mucosa, torturous colon. The advantages of CELS is the real time visualization of full thickness injury, avoids bowel resection, suture repair laparoscopic, invagination and mobilization of intestine. In recent review complication of CELS is coagulopathy (0–18%), and cancer risk of 2–10% (43). CELS has advantage of short stay and less operating time, the success rate of CELS is 75%. The long term outcome of CELS is safe and effective (44). Additional surgery is not necessary if the tumour is early stage and margins are clear, but CELS need dedicated OR room, two skilled doctors, endoscopic suturing, preoperative preparation, frozen section and learning curve.

### Application of fluorescence imaging in colorectal surgery

Anastomotic leak in colorectal surgery is major concern in terms of mortality and morbidity and long term outcomes. Most of the anastomotic leak occurs due to the inadequate perfusion at the anastomosis, there is no reliable tool to confirm the micro perfusion at time of anastomosis. Fluorescence angiography is a new tool introduced in laparoscopic MIS to assess the adequate perfusion at the time of anastomosis. PILLAR II multi-institutional



trial of 139 patients on use of fluorescence angiography showed that the success rate of angiography is 99% and by performing a fluorescence angiography study changed the planned proximal margin of transection in 7.9% of patients, with resulting leak rates of 0% (45). This is new technique and studies have showed safety and feasibility of this technique. This technique can be useful mainly where there is high risk anastomosis, and extended resections and resections of CRC where there is risk of precarious blood supply.

### **Natural orifice transluminal endoscopic surgery (NOTES) in rectal surgery**

The leading edge of minimal invasive surgery is NOTES. Organ preserving surgery has been the recent trend in rectal surgery which has less pelvic complications and no anastomotic leak when compared to radical surgery. Since the introduction of Transanal endoscopic surgery platform in 1980 by Dr. Gerhart Buess there has been many modification, in 2009 the technique of transanal minimally invasive surgery (TAMIS) was introduced by Dr. Mathew Albert. Transanal surgery is mainly performed for benign rectal lesions and T1 lesions. The advantage of NOTES is that it avoids stoma, and complications of anastomotic leak, and prevents neurovascular injury to bladder and preserves sexual function. Advantages of TEM is it has stable platform, specific insufflation, and dedicated suction and more proximal rectal lesions up to 20 cm can be resected, 3D vision. TAMIS has short learning curve as it has the similar instrumentation and techniques of SILS, decrease set up time for platform, flexibility of instruments use and better working angle for instruments. There is robust data on safety and feasibility of TEM/TAMIS, meta-analysis (46) compared three RCT concluded that TEM showed oncological outcomes equivalent to TME in early rectal cancer (cT1–2N0M0). TEM is also associated with a significantly shorter operative time, decreased intraoperative blood loss, decreased need for stoma and analgesia, and shorter hospital stay. TEM and TME were similar in terms of perioperative mortality and complete tumour resection. There are further CARTS, TESAR trial awaited to show whether there is advantage of transanal surgery in rectal cancer.

Trans anal total mesorectal excision (TaTME) is a new extension of MIS in treatment of rectal cancers. It can be performed as pure Transanal or hybrid procedure. The advantage of TaTME is in narrow pelvis, obese patients,

large rectal tumours, irradiated patients, reoperative surgery. It is a bottom up approach which helps in clear visualization of rectum and mesorectum. Till now less than 500 cases have been reported which showed safety and feasibility of the procedure, recent systematic review (47) showed TaTME has good quality specimens with CRM clear in 98% and 1% LR in 14-month follow up, long term outcomes are still awaited. Further on-going COLOR III trial is awaited to know the long term outcomes.

### **Summary**

Minimal invasive surgery in colorectal cancer results in good short term benefits with equivalent long term outcomes compared to open surgery. CME produces better quality specimen and showing promising long term outcomes, further studies need to address the long term benefit of CME. Robotic rectal surgery is an emerging technique with advantage in low rectal cancer, male pelvis and in obese patients. Trans anal surgery is a new platform in management of rectal cancer.

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