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Feasibility and oncological outcomes of laparoscopic rectal resection following neo-adjuvant chemo-radiotherapy: A systematic review

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Data sharing: This is a systematic review and all data pertaining to the study have been summarized in the tables of the manuscript. No additional data are available.

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Abstract

AIM: To study the feasibility and oncological outcomes following laparoscopic total mesorectal excision (LTME) in patients who have received Neo-adjuvant long course chemo-radiotherapy (LCRT).

METHODS: A protocol driven systematic review of published literature was undertaken to assess the feasibility and oncological outcomes following LTME in patients receiving LCRT. The feasibility was assessed using peri-operative outcomes and short term results. The oncological outcomes were assessed using local recurrence, disease free survival and overall survival.

RESULTS: Only 8 studies-1 randomized controlled trial, 4 Case Matched/Controlled Studies and 3 Case Series were identified matching the search criteria. The conversion rate was low (1.2% to 28.1%), anastomotic leak rates were similar to open total mesorectal excision (0%-4.1% *vs* 0%-8.3%). Only 3 studies reported on local recurrence rates (5.2%-7.6%) at median 34 mo follow-up. A single study described disease free survival and overall survival at 3 years as 78.8% and 92.1% respectively.

CONCLUSION: LTME following LCRT is feasible in experienced hands, with acceptable short term surgical outcomes and with the usual benefits associated with minimally invasive procedures. The long term oncological outcomes of LTME after LCRT appear to be comparable to open procedures but need further investigation.

Key words: Laparoscopic total mesorectal excision; Rectal adenocarcinoma; Feasibility; Outcomes; Neo-adjuvant chemo-radiotherapy

Core tip: Laparoscopic total mesorectal excision (LTME) following long course chemo-radiotherapy (LCRT) is

feasible in experienced hands, with acceptable short term surgical outcomes and with the usual benefits associated with minimally invasive procedures. The long term oncological outcomes of LTME after LCRT appear to be comparable to open procedures but need further investigation.

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INTRODUCTION

Total Mesorectal Excision using an open approach (OTME) is now accepted as the gold standard for treatment rectal cancer[1]. In recent years, since the medical research council United Kingdom trial, neo-adjuvant long course chemo-radiotherapy is being routinely used as a part of treatment of locally advanced mid and low rectal cancers[2]. Laparoscopic rectal resection has been shown to have superior short term outcomes compared to open resections. However, long term oncological results are still debated[3]. In addition, it is generally accepted that laparoscopic low rectal resection and Abdomino-perineal resections (APR) are technically challenging[4].

Most trials comparing laparoscopic and open resections for rectal cancer suggest that laparoscopic rectal resections are technically feasible however, short and long term outcomes in this group are difficult to determine[5,6]. Also, laparoscopic total mesorectal excision (LTME) following neo-adjuvant chemo-radiotherapy (LCRT) is oncologically and technically challenging due to tissue fibrosis and scarring[7].

This systematic review addresses the feasibility and outcome of laparoscopic rectal resection following neo-adjuvant chemo-radiotherapy. There is no level 1 evidence addressing this and to the best of our knowledge there is no structured review of the published literature on this topic.

MATERIALS AND METHODS

A systematic review of literature was performed as per the protocol described below to address the issue of feasibility of laparoscopic TME following neo-adjuvant chemo-radiotherapy. PubMed, Cochrane, Embase, OVID, and CINAHL were searched for articles published between Jan 2004 to June 2014 using the search criteria as described in Table 1.

The keywords for search were laparoscopy, minimally invasive surgery, open, rectum, cancer, abdomino-perineal resection, anterior resection, colorectal neoplasms, rectal neoplasms, rectal adenocarcinoma, rectal cancer, neo-adjuvant chemo-radiotherapy, proctectomy, and total mesorectal excision. Search was done as free text words and in their variable combinations.

Table 1 Search strategy

Search strategy
1 Rectal adenocarcinoma - tracked to MeSH to include all subheadings and combining with OR and clicking the Explode box; limit to English language and Humans - no time limits selected
2 Surgery - tracked to MeSH to include all subheadings and combining with OR and clicking the Explode box; limit to English language and Humans - no time limits selected
3 Laparoscopy - tracked to MeSH to include all subheadings and combining with OR and clicking Explode box; limit to English language and Humans - no time limits selected
4 Minimally invasive surgery - tracked to MeSH to include all subheadings and combining with OR and clicking Explode box; limit to English language and Humans - no time limits selected
5 Anterior Resection - Keyword search only (not linked to MeSH headings)
6 Neo-adjuvant chemo-radiotherapy
7 Proctectomy - Keyword search only (not linked to MeSH headings)
8 Total Mesorectal Excision - Keyword search only (not linked to MESH headings)
9 Combine 1 and 2 and 5 and 6 and 7 and 8
10 Combine 1 and 3 and 4 and 5 and 6 and 7 and 8

Study selection

The retrieved results were screened by two authors (Dhruva Rao PK and Nair MS) using the title and abstracts against the inclusion and exclusion criteria as described below. Any studies that did not have published abstracts were excluded. Full text articles of potentially relevant studies were obtained and assessed independently by two authors (Dhruva Rao PK and Nair MS) considering the inclusion and exclusion criteria for review. All references of all guideline articles and review articles were searched to identify any potential articles not already identified. Disagreements were resolved through discussion and by involving the third author (Haray PN).

Inclusion criteria

Randomized studies comparing open and laparoscopic rectal resection following neo-adjuvant chemo-radiotherapy for rectal adenocarcinoma; Case matched series comparing LTME with OTME following neo-adjuvant chemo-radiotherapy for rectal adenocarcinoma; Case control studies comparing LTME with OTME following neo-adjuvant chemo-radiotherapy for rectal adenocarcinoma; Case series with > 20 patients from tertiary centres; Published in English language; Feasibility studies of laparoscopic rectal resections for cancer including historical control cohorts.

Exclusion criteria

Study groups were not clearly defined; Studies in whom the "cancer" group cannot be separated; Studies comparing resections performed for benign indications only; Studies including local resections

Table 2 Overview of studies with extractable data

Ref.	Year	Country	Type of study	Total No. of patients	Patients Lap	Patients open
Kang *et al*[9]	2010	South Korea	RCT	340	170	170
Kusano *et al*[11]	2014	Japan	Case control Study	33	19	14
Hu *et al*[14]	2013	China	Case control Study	137	51	86
Seshadri *et al*[12]	2011	India	Case control Study	144	72	72
Denoya *et al*[15]	2009	United States	Case matched series	64	32	32
[1]Saklani *et al*[13]	2013	South Korea	Case series	64	64	NA
[1]Denost *et al*[10]	2011	France	Case series	292	292	NA
Motson *et al*[7]	2011	United Kingdom	Case series	26	26	NA

[1]Data pertaining to LCRT + laparoscopic resection group of the study only extracted therefore treated as case series. NA: Not applicable; LCRT: Long course chemo-radiotherapy; RCT: Randomized controlled trial.

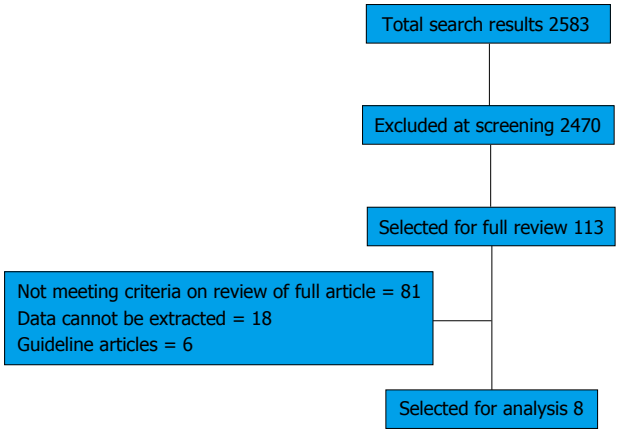

Figure 1 PRISMA flow diagram.

(trans-anal endoscopic microsurgery, trans-anal excision) but the major resection group cannot be separated; the outcomes of interest defined below were not reported or it was impossible to determine them from the published results; the surgical procedures were performed by surgical trainees or by surgeons during the learning curve for laparoscopic or conventional rectal surgery.

Data extraction

A structured proforma was used for data extraction for the patients undergoing laparoscopic resection after neo-adjuvant long course chemo-radiotherapy only. No attempt was made to contact the authors of studies if inadequate amount of information was available and such studies were excluded.

Outcome measures/end-points

We have assessed 2 sets of outcomes.

For feasibility assessment, we have considered estimated blood loss, ureteral injuries, other collateral injuries, overall peri-operative morbidity, length of hospital stay, anastomotic leakage, intra-abdominal abscess, urinary retention, postoperative ileus, 30 d mortality. We have also assessed circumferential/radial resection margin (CRM) and lymph node harvest.

For oncological outcome assessment, we have considered loco-regional recurrence, metachronous distant metastasis, disease free survival (DFS) and overall survival.

Statistical analysis

Prior to pooled analysis, the studies must pass 2 assessments of heterogeneity - qualitative and quantitative[8]. Qualitative assessment is based on 4 key concepts of study design (Patients, Interventions, Outcomes and Study Types). If studies are deemed heterogeneous on this assessment, it is inappropriate to proceed to quantitative assessment using statistical tests such as χ^2 test or Cochrane Q, *etc.*[8]. In this review the studies were deemed heterogeneous based on the above mentioned qualitative criteria and so we did not proceed to statistical analysis.

RESULTS

The initial search identified 2583 studies (Figure 1). Two thousand four hundred and seventy were excluded after initial screening of titles and abstracts. The remaining 113 studies were critically reviewed using the full article. Of these, 26 articles met the inclusion criteria and reviewed in detail. However, data relevant to this review could be extracted from only 8 studies (Table 2). Table 3 summarizes the 18 studies from which adequate extraction of appropriate data was not possible.

The selected publications included a combination of randomized controlled trial (RCT) and non RCT. Qualitative assessment of the studies revealed: (1) Type of studies identified were clearly heterogeneous (Table 2); (2) Patient selection criteria for LCRT were different in the different studies (Table 4); and (3) The LCRT regimen patients received was also different (Table 4).

Thus the studies were heterogeneous in terms of Study Design, Patient Groups and Interventions. Due to this heterogeneity, a pooled analysis or meta-analysis was considered inappropriate and hence was not carried out.

Of the 8 studies included, one was a RCT and 4 were case controlled studies or case matched series. The number of patients in the Laparoscopic group in the selected studies range from 19 to 292. The

Table 3 Studies from which data could not be extracted (sub group analysis not described/reported)

Ref.	Year	Country	Type of study	Percent having LCRT in Lap group
van der Pas *et al*[5]	2013	The Netherlands	RCT[1]	59
Lujan *et al*[6]	2009	Spain	RCT	72.3
Lujan *et al*[16]	2013	Spain	Case Control	58.1
McKay *et al*[17]	2012	Australia	Case Control	48.8
Laurent *et al*[18]	2011	France	Case Control	93.6
Patel *et al*[19]	2011	United States	Case Matched	50
Li *et al*[20]	2011	China	Case Control	34.5
Kellokumpu *et al*[21]	2011	Finland	Case Control	34
Greenblatt *et al*[22]	2011	United States	Case Control	31.6
da Luz Moreira *et al*[23]	2011	United States	Case Matched	33
Baik *et al*[24]	2010	United States	Case Matched	79.6
Westerholm *et al*[25]	2012	Canada	Case Series	7.4
Jefferies *et al*[26]	2011	United Kingdom	Case Series	43.8
Glancy *et al*[27]	2011	United Kingdom	Case Series	8
Lam *et al*[28]	2010	Belgium	Case Series	56.7
Sartori *et al*[29]	2010	Italy	Case Series	39.1
Cheung *et al*[30]	2010	Hong Kong	Case Series	21.5
Park *et al*[31]	2010	South Korea	Case Series	8.1

[1]Patients in this trial had short course radio therapy. LCRT: Long course chemo-radiotherapy; RCT: Randomized controlled trial.

Table 4 Comparison of criteria for long course chemo-radiotherapy and regimes

Ref.	Staging imaging	Criteria for LCRT	Chemo agent	Rad dose/duration
Kang *et al*[9]	CT, MRI, ERUS	cT3N0-2 M0 Mid/low rectal cancer	I/V 5FU + leucovorin or oral capecitabine	50.4 Gy over 5.5 wk (tumour boost used)
Kusano *et al*[11]	CT, MRI	T3N0-3M0[2]	Different protocols	Total dose = 45 Gy/duration not reported
Hu *et al*[14]	CT, MRI, ERUS	Stage 2/3 tumours	Capecitabine and oxaliplatin	50 Gy over 5 wk
[1]Seshadri *et al*[12]	CT	T2/T3 N+, T4 excluded	Mitomycin and 5FU	Total dose = 50 Gy/duration not reported
Denoya *et al*[15]	CT, MRI, ERUS	T3/4 or N+ disease	5FU or Xeloda	Total dose = 50.4 Gy/duration not reported
Saklani *et al*[13]	NR	T3/4 or N+ disease	5FU	Total dose = 50.4 Gy/duration not reported
Denost *et al*[10]	CT, MRI, ERUS	T3/4 = 265 (90.8%), T1/2 = 27 (9.2%)	I/V 5FU and leucovorin	45 Gy over 5 wk
Motson *et al*[7]	CT, MRI	T3/4 N+ + involved/ threatened CRM	5FU or Uftoral	45/50 Gy over 5 wk (3/4 fields)

[1]7/72 (Lap) and 6/72 (open) received only RT; cannot separate data; [2]Using TNM classification of malignant tumours 7th edition 2009. NR: Not reported; LCRT: Long course chemo-radiotherapy; CT: Computed tomography; MRI: Magnetic resonance imaging; CRM: Circumferential/radial resection margin; ERUS: Endoluminal rectal ultra-sound.

only RCT (COREAN trial[9]) that we have been able to identify had 170 patients in the study arm. The study with largest number of patients with LTME following LCRT is from France with 292 patients[10].

The patient characteristics of all the studies are shown in Table 5. As can be seen from the table, they were mid or low rectal tumours. The APR rates varied from 11.2% to 89%. All studies had reported the imaging modalities and selection criteria for LCRT with the type and dose of chemo and radiotherapy (Table 4). There was wide heterogeneity in the type, dose and duration of LCRT among the studies.

Table 6 reports the peri-operative course. The interval between LCRT and surgery was reported by all except by one study[11] with the median minimum and maximum intervals being 6 and 8 wk respectively. The reported conversion rates from laparoscopic to open operations ranged from 1.2% to 28.1%. In the Laparoscopic arm, three of the eight identified studies reported a median estimated blood loss of 200 mL.

While only two studies reported intra operative complications (Table 6), all studies have reported post-operative complications (Table 7). In the studies where comparative data was available, the laparoscopic group had a low anastomotic leak rate compared to the open group (0%-4% *vs* 0%-8.3% respectively). The COREAN trial reported a higher leak rate for LTME *vs* OTME (1.2% *vs* 0% respectively). However, 2 case series reported anastomotic leak rates of 12.7%[10] and 18.7%[7]. Interestingly these had higher conversion rates as well (18.8%[10] and 11.5%[7] respectively). Pelvic abscess was also less in laparoscopic group compared to the open group (0%-10.5% *vs* 0.6%-14.2%). Post-operative ileus was less in Laparoscopic group (0%-10% *vs* 1.2%-12.9%). Post-operative voiding difficulty varied from 2%-10% in laparoscopic group compared to 2.3%-7.1% in open group.

The short term outcomes are summarized in Table 8. All except 2 studies have reported post-operative length of stay with the median stay ranging between

Table 5 Patient characteristics

Ref.	Age (yr)		Laparoscopic Group		Open Group		BMI		Distance from Anal Verge (cm)		Laparoscopic Group		Open Group	
	Lap	Open	Men	Women	Men	Women	Lap	Open	Lap	Open	AR	APR	AR	APR
[1]Kang *et al*[9]	57.8 (11.1)	59.1 (9.9)	64.7%	35.3%	64.7%	35.3%	24.1 (3.2)	24.1 (3.2)	5.6 (2.3)	5.3 (2.5)	151 (88.8%)	19 (11.2%)	146 (85.9%)	24 (14.1%)
Kusano *et al*[11]	58 (32-82)	55 (39-73)	15 (78.9%)	4 (21.1%)	8 (57.1%)	6 (42.9%)	⩽ 25 = 14 (73.7%) > 25 = 5 (26.3%)	⩽ 25 = 9 (64.3%) >25 = 5 (35.7%)	2 (0-50)	3.7 (0-10)	11 (57.9%)	8 (42.1%)	4 (28.6%)	10 (71.4%)
Hu *et al*[14]	55 (35-78)	55 (29-82)	34 (66.7%)	17 (33.3%)	56 (65.1%)	30 (34.9%)	23.4 (16-31.2)	24.2 (16.3-36.2)	⩽ 5 = 33 (64.7%) > 5 = 18 (35.3%)	⩽ 5 = 54 (62.8%) > 5 = 32 (37.2%)	32 (62.7%)	18 (35.3%)	36 (41.9%)	44 (51.2%)
Seshadri *et al*[12]	48 (22-73)	48 (19-71)	47 (65%)	25 (35%)	45 (62%)	27 (38%)	21 (15-33)	22 (14-38)	3 (0-8)	3 (0-10)	8 (11%)	64 (89%)	8 (11%)	64 (89%)
[1]Denoya *et al*[15]	56.3	57.1	19 (59.4%)	13 (40.6%)	18 (56.3%)	14 (43.7%)	25	26.4	4.1	4.6	24 (75%)	8 (25%)	24 (75%)	8 (25%)
Denost *et al*[10]	65 (20-85)	NA	179 (61.3%)	113 (38.7%)	NA	NA	25 (16-39)	NA	< 5 = 175 (59.9%) > 5 = 117 (40.1%)	NA	NR	NR	NA	NA
Motson *et al*[7]	63 (39-81)	NA	21 (80.8%)	5 (19.2%)	NA	NA	NR	NA	< 5 = 11 (42.3%) > 5 = 15 (57.7%)	NA	16 (61.5%)	10 (38.5%)	NA	NA

Values reported as median (range) except [1]where it is Mean. NA: Not applicable; AR: Anterior resection; APR: Abdomino-perineal resection; BMI: Body mass index; NR: Not reported.

Table 6 Peri-operative outcomes

Ref.	Interval to surgery	Conversion	Estimated blood loss		Intra-op injury		Diversion stoma	
			Lap	Open	Lap	Open	Lap	Open
[1]Kang *et al*[9]	[2]6-8 wk	1.2%	Median - 200 mL	Median - 217.5 mL	Yes[1]	Yes[1]	91.4%	88.4%
Kusano *et al*[11]	NR	NR	< 200 mL = 47.4% > 200 = 52.6%	< 200 = 92.9% > 200 = 7.1%	NR	NR	NR	NR
Hu *et al*[14]	Mean 53 d (28-105 d)	5.9%	Mean 204.7 (80-1000 mL)	Mean 352.5 (100-1200) mL	No	Ureteric injury = 1.2%	NR	NR
Seshadri *et al*[12]	Median 8 (4-36) wk	4.1%	Median 200 (100-600) mL	Med 400 (150-1500) mL	NR	NR	NR	NR
Denoya *et al*[15]	Mean 6.5 wk	28.1%	Mean 313 ± 443	Mean 279 ± 229	NR	NR	75%	75%
Denost *et al*[10]	[2]6 wk	18.8%	NR	NA	NR	NA	81.2%	NA
Motson *et al*[7]	Median 11 wk	11.5%	NR	NA	NR	NA	75%	NA

[1]There were 3 patients in each group needing re-operation - indication for these were not described. Also, one patient in each group had a brachial plexus injury; [2]Study protocol - actual durations not mentioned. NR: Not reported; NA: Not applicable.

8-24 d for the laparoscopic group and 9-35 for the open group. Only 2 case series[7,10] reported procedure related mortality (0.3%-3.8%).

The markers of surgical quality are reported in Table 9. Only the COREAN trial[9] reported the TME quality with 72.4% of the resection as complete. One study[12] defined the CRM positivity as 2 mm while the others used the standard 1 mm measurement. The CRM positivity in the laparoscopic group was 1.3% to 2.9% and that for the open group was 3.5%-9.7%. The numbers of lymph nodes harvested did not differ between laparoscopic and open groups.

Only 3 studies reported a follow up period of 34 mo or above (Table 8). The rest had data on short term follow up with one study not reporting any follow up data. Local recurrence was reported as 5.2%-7.6% in the laparoscopic groups after 34 mo of follow up. Only one study reported comparative local recurrence between the laparoscopic and open groups (5.2% for laparoscopic *vs* 21.4% for open)[11]. Only one study[13] reported disease free survival and overall survival at 3 years (78.8% and 92.1 % respectively).

Table 7 Post-operative complications

Ref.	Anastomotic leak (%)		Pelvic abscess (%)		Post-op Ileus (%)		Acute voiding difficulty (%)		Stoma complications (%)	
	Lap	Open	Lap	Open	Lap	Open	Lap	Open	Lap	Open
Kang *et al*[9]	1.2	0	0	0.6	10	12.9	10	4.1	0.6	0
Kusano *et al*[11]	0	7.1	10.5	14.2	5.2	7.1	0	7.1	NR	NR
[2]Hu *et al*[14]	3.1	8.3	0	1.2	0	1.2	1.2	2.3	0	2
Seshadri *et al*[12]	4.1	8.3	NR	NR	NR	NR	11	7	NR	NR
Denoya *et al*[15]	NR	NR	NR	NR	5	5	NR	NR	NR	NR
Denost *et al*[10]	12.7	NA	NR	NA	NR	NA	NR	NA	NR	NA
[1]Motson *et al*[7]	18.7	NA	NR	NA	NR	NA	15.4	NA	NR	NA

[1]2 patients had adhesiolysis; [2]Other complications, Urinary fistula = 1 and Rectovaginal fistula = 1 both in open group. NR: Not reported; NA: Not applicable.

Table 8 Short term and long term outcomes

Ref.	Post-op length of stay		30 d mortality (%)	Length of follow-up	Local recurrence	
	Lap	Open			Lap	Open
Kang *et al*[9]	8 (7-12)	9 (8-12)	NR	3 mo	NA	NA
Kusano *et al*[11]	24 (14-92)	35 (14-70)	NR	Median 39 mo	1 (5.2%)	3 (21.4%)
Hu *et al*[14]	10 (6-34)	16 (6-44)	NR	Short term outcomes only	NA	NA
Seshadri *et al*[12]	12 (6-45)	15 (10-50)	None	Short term outcomes only	NA	NA
[1]Denoya *et al*[15]	6.1 ± 2.4	7.6 ± 2.3	NR	Short term outcomes only	NA	NA
Denost *et al*[10]	NR	NA	0.3	NR	NR	NA
Motson *et al*[7]	8 (5-17)	NA	3.8	Median 34 mo	2 (7.6%)	NA
Saklani *et al*[13]	NR	NA	NR	Median 36 mo	4 (6.3%)	NA

Reported as median (range) except [1]where it is mean. NR: Not reported; NA: Not applicable.

Table 9 Quality markers

Ref.	CRM positivity		Lymph node harvest[1]	
	Lap	Open	Lap	Open
Kang *et al*[9]	2.9%	4.1%	17 (12-22)	18 (13-24)
[3]Kusano *et al*[11]	NR	NR	< 12 = 73.7% > 12 = 26.3%	< 12 = 64.3% > 12 = 35.7%
Hu *et al*[14]	1.9%	3.5%	12 (2-20)	11 (1-25)
[4]Seshadri *et al*[12]	1.3%	9.7%	7 (1-24)	7 (1-25)
Denoya *et al*[15]	Yes[5]	Yes[5]	19 ± 9[2]	19 ± 9[2]
Denost *et al*[10]	NR	NA	NR	NA
[6]Motson *et al*[7]	Yes[6]	NA	5 (0-14)	NA

[1]Lymph node harvest reported as median (range) except [2]where it is mean and [3]where it is percent of patients with node count < or > 12; [4]Authors define CRM as 2 mm; [3]Authors report negative "radical" resection margins in all patients in discussion; [5]CRM reported as Lap 1.17 ± 0.7; Open 0.96 ± 0.5; [6]CRM reported as 5.5 mm (< 1-15 mm). NR: Not reported; NA: Not applicable; CRM: Circumferential resection margins.

DISCUSSION

The studies were heterogeneous. In spite of this, the reported short term outcomes for LTME were not inferior to OTME. Available data shows LTME offers the same short term advantages in outcomes like estimated blood loss, other collateral injuries, overall intra-operative morbidity, post-operative length of stay, intra-abdominal abscess and post-operative ileus even after LCRT. Short term surrogate measures of oncologic parameters are at least equal to the open procedure.

LCRT makes the normal anatomical planes within the pelvis challenging due to tissue fibrosis and scarring. The tissue planes can be more difficult to follow compared with non-irradiated cases[7].

The magnified view of operative field and the improving technology with efficient energy devices in addition to meticulous attention to haemostasis to maintain good views during LMTE are factors that help reduce the blood loss as reflected in the reported estimated blood loss of these studies. Pelvic abscess was also less in laparoscopic group compared to open. This may be due to the fact that the blood loss is less with consequent less postoperative haematoma, *etc*.

Irradiation causes fibrosis and ischaemia[10] and increases the thickness of the rectal wall making a safe rectal division by stapling devices technically more difficult[10]. It is also thought to increase the risk of anastomotic leak. However, the reported anastomotic leak rate in LTME was generally low. One study[7] reported a higher leak rate (18.7%) but this is probably due to low number of patients in this study.

The surrogate markers of oncological outcome like lymph node harvest, positivity of CRM margins with LTME were comparable and not inferior to both contemporaneous open procedures as well as historically reported data.

The only RCT identified, the COREAN trial[9], randomised 340 patients after LCRT to LTME or OTME. It observed no difference between CRM positivity, macroscopic quality of the total mesorectal excision, number of harvested lymph nodes or perioperative morbidity between the two groups[9]. The short term benefits were better in LTME. This trial demonstrated LTME after LCRT was safe in the hands of experienced

surgeons (participating surgeons had a median experience of 75 LTMEs). Although this trial was not sufficiently powered to address survival outcomes (one of the limitations of this trial), the long term outcome from COREAN trial is expected to shed more light on the oncological effectiveness of LTME in this group of rectal cancer patients.

The other end-points of this review were the local recurrence rates, and DFS. These results are based on case controlled study or data from experienced tertiary centres. The rate of local recurrence varied from 5.2% to 7.6% in the LTME group. Only one study[11] reported comparative data for OTME (21.4%). Only one study reported DFS of 78.8% in LTME after 3 years of follow up. Unfortunately this did not report on a similar figure for OTME[13].

We identified 18 other studies which had a subgroup of patients who underwent LCRT followed by laparoscopic rectal resection. However, insufficient data were included for relevant data extraction and analysis. An analysis of the raw data from these published studies may provide interim results quicker. However, such an exercise would require the co-operation of various authors from around the world to contribute their data to help create an international registry for analysis: this is unlikely to be feasible retrospectively. Hence, a prospective, multicentre randomised trial recruiting patients from appropriate centres and adequately powered to address survival outcomes is needed to answer the question of oncological effectiveness.

Although there is paucity of published data on the rates of local and distant disease recurrence (Disease Free Survival) following LTME after LCRT, available data shows LTME following LCRT is not inferior to open TME with the inherent advantages of Laparoscopic surgery.

LTME is feasible in experienced hands, with acceptable short term surgical outcomes and with the usual benefits associated with minimally invasive procedures. The long term oncological outcomes of LTME after LCRT appear to be comparable to open procedures but need further investigation probably with a well-designed adequately powered multicentre trial.

COMMENTS

Background

Laparoscopic total mesorectal excision (LTME) has been shown to be feasible with acceptable short and intermediate term results in management of rectal cancers. However, the increasing use of neo-adjuvant long course chemo-radiotherapy (LCRT), and the resultant increased fibrosis and alterations to the tissue planes has increased the challenges of the LTME. To the authors' knowledge, there is no level 1 evidence to support its use.

Research frontiers

Over the recent years, numerous publications addressing this area of rectal cancer management have been published. The authors aimed to conduct a systematic review of the published literature to inform future practice.

Innovations and breakthroughs

This systematic review has shown that LTME in patients undergoing LCRT is feasible with acceptable short and intermediate term surgical and oncological outcomes in experienced hands. It has also identified the need for a sufficiently powered RCT to address this issue. In the interim, this study which has assimilated and analysed the raw data from various publications could provide useful information on the subject.

Applications

This review lends support to the practice of LTME in experienced centres within the multimodal approach to rectal cancer. However, long term outcomes (as in all oncological treatments) need to be continuously monitored.

Terminology

Total mesorectal excision (TME): this is the gold standard surgical technique for the management of mid to low rectal cancers and involves the complete removal of the rectum and mesorectal tissue. As it is traditionally performed by an open approach, it can also be called open TME. Laparoscopic TME: Using the laparoscopic approach to perform TME. LCRT: Use of pre-operative course of radiotherapy with potentiating chemotherapy (neo-adjuvant treatment) over a few weeks, usually a 5 wk cycle. Following the chemo-radiation, surgery in the form of TME is performed after a delay of several weeks. The aim is to shrink the tumour or "sterilize" the circumferential resection margin.

Peer-review

This review addresses a very interesting and timely clinical issue.

REFERENCES

1 **Enker WE**. Total mesorectal excision--the new golden standard of surgery for rectal cancer. *Ann Med* 1997; **29**: 127-133 [PMID: 9187227 DOI: 10.3109/07853899709113698]

2 **Foster JD**, Jones EL, Falk S, Cooper EJ, Francis NK. Timing of surgery after long-course neoadjuvant chemoradiotherapy for rectal cancer: a systematic review of the literature. *Dis Colon Rectum* 2013; **56**: 921-930 [PMID: 23739201 DOI: 10.1097/DCR.0b013e31828aedcb]

3 **Shussman N**, Wexner SD. Current status of laparoscopy for the treatment of rectal cancer. *World J Gastroenterol* 2014; **20**: 15125-15134 [PMID: 25386061]

4 **Lee JK**, Delaney CP, Lipman JM. Current state of the art in laparoscopic colorectal surgery for cancer: Update on the multi-centric international trials. *Ann Surg Innov Res* 2012; **6**: 5 [PMID: 22846394]

5 **van der Pas MH**, Haglind E, Cuesta MA, Fürst A, Lacy AM, Hop WC, Bonjer HJ. Laparoscopic versus open surgery for rectal cancer (COLOR II): short-term outcomes of a randomised, phase 3 trial. *Lancet Oncol* 2013; **14**: 210-218 [PMID: 23395398 DOI: 10.1016/S1470-2045(13)70016-0]

6 **Lujan J**, Valero G, Hernandez Q, Sanchez A, Frutos MD, Parrilla P. Randomized clinical trial comparing laparoscopic and open surgery in patients with rectal cancer. *Br J Surg* 2009; **96**: 982-989 [PMID: 19644973 DOI: 10.1002/bjs.6662]

7 **Motson RW**, Khan JS, Arulampalam TH, Austin RC, Lacey N, Sizer B. Laparoscopic total mesorectal excision following long course chemoradiotherapy for locally advanced rectal cancer. *Surg Endosc* 2011; **25**: 1753-1760 [PMID: 21533976 DOI: 10.1007/s00464-010-1353-y]

8 **Hatala R**, Keitz S, Wyer P, Guyatt G. Tips for learners of evidence-based medicine: 4. Assessing heterogeneity of primary studies in systematic reviews and whether to combine their results. *CMAJ* 2005; **172**: 661-665 [PMID: 15738493 DOI: 10.1503/cmaj.1031920]

9 **Kang SB**, Park JW, Jeong SY, Nam BH, Choi HS, Kim DW, Lim SB, Lee TG, Kim DY, Kim JS, Chang HJ, Lee HS, Kim SY, Jung KH, Hong YS, Kim JH, Sohn DK, Kim DH, Oh JH. 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**: 637-645 [PMID: 20610322 DOI: 10.1016/S1470-2045(10)70131-5]

10 **Denost Q**, Laurent C, Paumet T, Quintane L, Martenot M, Rullier E. Laparoscopic surgery for rectal cancer: preoperative radiochemotherapy versus surgery alone. *Surg Endosc* 2012; **26**: 1878-1883 [PMID: 22219008 DOI: 10.1007/s00464-011-2119-x]

11 **Kusano T**, Inomata M, Hiratsuka T, Akagi T, Ueda Y, Tojigamori M, Shiroshita H, Etoh T, Shiraishi N, Kitano S. A comparison of laparoscopic and open surgery following pre-operative chemoradiation therapy for locally advanced lower rectal cancer. *Jpn J Clin Oncol*

2014; **44**: 305-310 [PMID: 24596335]
12 **Seshadri RA**, Srinivasan A, Tapkire R, Swaminathan R. Laparoscopic versus open surgery for rectal cancer after neoadjuvant chemoradiation: a matched case-control study of short-term outcomes. *Surg Endosc* 2012; **26**: 154-161 [PMID: 21792713]
13 **Saklani AP**, Lim DR, Hur H, Min BS, Baik SH, Lee KY, Kim NK. Robotic versus laparoscopic surgery for mid-low rectal cancer after neoadjuvant chemoradiation therapy: comparison of oncologic outcomes. *Int J Colorectal Dis* 2013; **28**: 1689-1698 [PMID: 23948968 DOI: 10.1007/s00384-013-1756-z]
14 **Hu JJ**, Liang JW, Wang Z, Zhang XM, Zhou HT, Hou HR, Zhou ZX. Short-term outcomes of laparoscopically assisted surgery for rectal cancer following neoadjuvant chemoradiotherapy: a single-center experience. *J Surg Res* 2014; **187**: 438-444 [PMID: 24252856 DOI: 10.1016/j.jss.2013.10.039]
15 **Denoya P**, Wang H, Sands D, Nogueras J, Weiss E, Wexner SD. Short-term outcomes of laparoscopic total mesorectal excision following neoadjuvant chemoradiotherapy. *Surg Endosc* 2010; **24**: 933-938 [PMID: 19851807 DOI: 10.1007/s00464-009-0702-1]
16 **Lujan J**, Valero G, Biondo S, Espin E, Parrilla P, Ortiz H. Laparoscopic versus open surgery for rectal cancer: results of a prospective multicentre analysis of 4,970 patients. *Surg Endosc* 2013; **27**: 295-302 [PMID: 22736289 DOI: 10.1007/s00464-012-2444-8]
17 **McKay GD**, Morgan MJ, Wong SK, Gatenby AH, Fulham SB, Ahmed KW, Toh JW, Hanna M, Hitos K. Improved short-term outcomes of laparoscopic versus open resection for colon and rectal cancer in an area health service: a multicenter study. *Dis Colon Rectum* 2012; **55**: 42-50 [PMID: 22156866 DOI: 10.1097/DCR.0b013e318239341f]
18 **Laurent C**, Paumet T, Leblanc F, Denost Q, Rullier E. Intersphincteric resection for low rectal cancer: laparoscopic vs open surgery approach. *Colorectal Dis* 2012; **14**: 35-41; discussion 42-43 [PMID: 21114752 DOI: 10.1111/j.1463-1318.2010.02528.x]
19 **Patel CB**, Ragupathi M, Ramos-Valadez DI, Haas EM. A three-arm (laparoscopic, hand-assisted, and robotic) matched-case analysis of intraoperative and postoperative outcomes in minimally invasive colorectal surgery. *Dis Colon Rectum* 2011; **54**: 144-150 [PMID: 21228660 DOI: 10.1007/DCR.0b013e3181fec377]
20 **Li S**, Chi P, Lin H, Lu X, Huang Y. Long-term outcomes of laparoscopic surgery versus open resection for middle and lower rectal cancer: an NTCLES study. *Surg Endosc* 2011; **25**: 3175-3182 [PMID: 21487864 DOI: 10.1007/s00464-011-1683-4]
21 **Kellokumpu IH**, Kairaluoma MI, Nuorva KP, Kautiainen HJ, Jantunen IT. Short- and long-term outcome following laparoscopic versus open resection for carcinoma of the rectum in the multimodal setting. *Dis Colon Rectum* 2012; **55**: 854-863 [PMID: 22810470 DOI: 10.1097/DCR.0b013e31825b9052]
22 **Greenblatt DY**, Rajamanickam V, Pugely AJ, Heise CP, Foley EF, Kennedy GD. Short-term outcomes after laparoscopic-assisted proctectomy for rectal cancer: results from the ACS NSQIP. *J Am Coll Surg* 2011; **212**: 844-854 [PMID: 21414814 DOI: 10.1016/j.jamcollsurg.2011.01.005]
23 **da Luz Moreira A**, Mor I, Geisler DP, Remzi FH, Kiran RP. Laparoscopic resection for rectal cancer: a case-matched study. *Surg Endosc* 2011; **25**: 278-283 [PMID: 20585962 DOI: 10.1007/s00464-010-1174-z]
24 **Baik SH**, Gincherman M, Mutch MG, Birnbaum EH, Fleshman JW. Laparoscopic vs open resection for patients with rectal cancer: comparison of perioperative outcomes and long-term survival. *Dis Colon Rectum* 2011; **54**: 6-14 [PMID: 21160307 DOI: 10.1007/DCR.0b013e3181fd19d0]
25 **Westerholm J**, Garcia-Osogobio S, Farrokhyar F, Cadeddu M, Anvari M. Midterm outcomes of laparoscopic surgery for rectal cancer. *Surg Innov* 2012; **19**: 81-88 [PMID: 22604576 DOI: 10.1177/1553350611415868]
26 **Jefferies MT**, Evans MD, Hilton J, Chandrasekaran TV, Beynon J, Khot U. Oncological outcome after laparoscopic abdominoperineal excision of the rectum. *Colorectal Dis* 2012; **14**: 967-971 [PMID: 22066511 DOI: 10.1111/j.1463-1318.2011.02882.x]
27 **Glancy DG**, Chaudhray BN, Greenslade GL, Dixon AR. Laparoscopic total mesorectal excision can be performed on a nonselective basis in patients with rectal cancer with excellent medium-term results. *Colorectal Dis* 2012; **14**: 453-457 [PMID: 21689350 DOI: 10.1111/j.1463-1318.2011.02682.x]
28 **Lam HD**, Stefano M, Tran-Ba T, Tinton N, Cambier E, Navez B. Laparoscopic versus open techniques in rectal cancer surgery: a retrospective analysis of 121 sphincter-saving procedures in a single institution. *Surg Endosc* 2011; **25**: 454-462 [PMID: 20607562 DOI: 10.1007/s00464-010-1191-y]
29 **Sartori CA**, Dal Pozzo A, Franzato B, Balduino M, Sartori A, Baiocchi GL. Laparoscopic total mesorectal excision for rectal cancer: experience of a single center with a series of 174 patients. *Surg Endosc* 2011; **25**: 508-514 [PMID: 20607560 DOI: 10.1007/s00464-010-1202-z]
30 **Cheung HY**, Ng KH, Leung AL, Chung CC, Yau KK, Li MK. Laparoscopic sphincter-preserving total mesorectal excision: 10-year report. *Colorectal Dis* 2011; **13**: 627-631 [PMID: 20163425 DOI: 10.1111/j.1463-1318.2010.02235.x]
31 **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**: 3195-3202 [PMID: 20589436 DOI: 10.1245/s10434-010-1162-5]

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