



Original article

Total mesorectal excision with or without lateral pelvic lymph node dissection for management of locally advanced low cancer rectum

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ABSTRACT

Background: there a conflicting results about the best approach of management of rectal cancer with lateral lymph nodes metastases and the role of performing lateral pelvic lymph nodes dissection in addition to total mesorectal excision in rectal cancer patient in improving patients' oncological outcomes is still uncertain.

Aim of the study was to correlate between performing lateral lymph nodes dissection in addition to total mesorectal excision and performing total mesorectal excision alone with neo-adjuvant therapy in patients with low rectal cancer.

Patients and methods: all patients with histologically confirmed low cancer rectum stages II and III, located below the level of the peritoneal reflection, aged from 20-85 years with no previous chemo-radiotherapy or pelvic surgery. We randomly divided patients who met the inclusion criteria into 2 groups the first group underwent total mesorectal excision in addition to lateral lymph nodes dissection while the second group underwent only total mesorectal excision alone with neo-adjuvant therapy. Operative, perioperative and oncological outcomes were assessed.

Results: we showed that the operative time of total mesorectal excision in addition to lateral lymph node dissection was longer and resulted in more blood loss than total mesorectal excision only ($p < 0.001$). Local recurrence rates ($p = 0.008$ and 0.022), disease free survival rates ($p = 0.27$) and overall survival rates ($p = 0.047$ and 0.001) were more favorable in patients underwent total mesorectal excision and lateral pelvic lymph nodes dissection than patients underwent total mesorectal excision alone. **Conclusions:** for patients with advanced low cancer rectum total mesorectal excision and lateral pelvic lymph nodes dissection decreased incidence of local recurrence and improved patients' survival than total mesorectal excision only.

Introduction

Cancer rectum, accounts for about 33% of all large bowel cancer and its prevalence is higher in elderly males [1]. Total mesorectal resection which was primarily described by Heald et al. [2], is the gold standard surgical management procedure which leads to a lower incidence of disease recurrence and favorable patients' survival rates [3].

Occurrence of spread to the lateral pelvic lymph nodes was found in about 25% of rectal cancer cases and it resulted from the drainage of the rectum lymphatic along the inferior mesenteric and the iliac arteries [4]. Spread to pelvic lymphatic and lymph nodes leads to a higher incidence of disease recurrence and dismal outcome [5]. There a conflicting results about the best approach of management of these lymphatic nodes metastases which aim at preventing disease recurrence and improving patients outcome [4].

Some Japanese surgeons encourage performing lateral lymph node dissection in addition to conventional mesorectal dissection of rectal cancer as they considered such lymph nodes invasion as a local disease [6]. On the contrary, according to recent TNM staging of the American Joint Committee on Cancer (AJCC) 8th edition, pelvic lymph nodes metastases could be considered a distant disease [7], so other western authors suggest using neoadjuvant radiochemotherapy instead of surgical excision so as to avoid patients morbidity that could result from lateral pelvic lymph nodes dissection [8]. It was found that dissection of the lateral pelvic lymph nodes has many disadvantages of increasing sexual and urinary dysfunction giving no significant oncological advantages [9]. Neo-adjuvant therapy was showed to be insufficient for adequate management of metastases to pelvic lymph nodes with higher incidence of disease recurrence in rectal cancer patients that were managed by total mesorectal excision and neo-adjuvant therapy than patients managed with by total mesorectal excision in addition to dissection of the lateral pelvic lymph nodes [10].

So the role of performing lateral pelvic lymph nodes dissection in addition to total mesorectal excision in rectal cancer patient in improving patients' oncological outcomes is still uncertain.

In the current study we aimed to correlate between performing lateral lymph nodes dissection

in addition to total mesorectal excision and performing total mesorectal excision alone with neo-adjuvant therapy in patients with low rectal cancer.

Designation of the study and included patients

Inclusion criteria:

All patients with histologically confirmed low cancer rectum stages II and III, located below the level of the peritoneal reflection, aged from 20-85 years with no previous chemo-radiotherapy or pelvic surgery.

Patients were admitted to General Surgery Department, Faculty of Medicine, Zagazig University in the period from May 2015 to June 2020.

We have acquired informed written consents from all operated patients before inclusion in the study and the institutional review board of Faculty of Medicine, Zagazig University approved the study design.

Exclusion criteria

Patients with clinical and radiological evidence of pelvic lymph nodes metastases, patients with distant metastases, concurrent or multiple cancers were excluded from the study. Patients with cancer spread to neighboring organs.

We randomly divided patients who met the inclusion criteria into 2 groups the first group underwent total mesorectal excision in addition to lateral lymph nodes dissection while the second group underwent only total mesorectal excision alone with neo-adjuvant therapy.

We assessed the clinical stage by digital rectal, radiological and endoscopic examination. Patients' clinicopathological, perioperative and follow-up data were recorded.

Surgical Procedures

We performed mesorectal excision by rectal mobilization, kept a plane around the mesorectum which has been resected about 4-cm distal to the cancer. If we found that the distal length of the mesorectum less than four cm distal to the tumor, we will perform total resection of the mesorectum. We have ligated the inferior mesenteric artery, in the case that we found inadequacy of distal colonic blood supply we could preserve left colonic artery after dissection of the lymph nodes.

We have dissected all groups of the lateral pelvic lymph nodes after performing total mesorectal excision.

We preserved the autonomic nerves as occurrence of metastases in the lymph nodes around nerves is rare.

Patient with stage III were given adjuvant chemotherapy (5-FU and L-leucovorin, but no patients in our study were given adjuvant radiotherapy. Time of operation, incidence of blood loss, hospital stay time, associated morbidities, complications after operation and death occur within thirty days after operation. After follow-up of patients' recurrence, progression and survival rates were detected.

Evaluation of relapse was done by digital examination and radiological evaluation.

We classified sites of local recurrence sites into three sites: central, lateral pelvis, and at site of the anastomosis.

During the 1st two years after the operation we evaluated tumor markers, CT or MRI on the chest, abdomen and pelvic every 4 months, then every 6 months.

RESULTS

Patient clinical data and pathological characteristics were nearly the same in both included groups (Table 1).

Regarding operative findings, we showed that the operative time of total mesorectal excision in addition to lateral lymph node dissection was longer and resulted in more blood loss than total mesorectal excision only (table 2) ($p < 0.001$).

We found no significant differences between patients regarding other perioperative events.

Oncological and follow-up findings

Local recurrence rates ($p = 0.008$ and 0.022), disease free survival rates ($p = 0.27$) and overall survival rates ($p = 0.047$ and 0.001) were more favorable in patients underwent total mesorectal excision and lateral pelvic lymph nodes dissection than patients underwent total mesorectal excision alone. Table 3

Table 1. Age Comparison between Total Mesorectal Excision (TME) With Lateral Pelvic Lymph Node Dissection (LPLD) and Total Mesorectal Excision (TME) alone for Management of Locally Advanced Low Cancer Rectum regarding demographic, pathological, operative, postoperative data and tumor markers:

Variables	Total	Surgical technique		p
		TME and LPLD	TME	
	N=80 (%)	N=40 (%)	N=40 (%)	
Age (years): Mean \pm SD Range	56.78 \pm 12.14 50 - 80	56.3 \pm 12.18 48 - 75	57.25 \pm 12.41 53 - 80	0.808
Gender: Male Female	56 (70) 24 (30)	28 (50) 12(50)	28 (50) 12 (50)	1
Size of the tumor (cm): < 5 cm \geq 5 - 10 cm	26 (32.5) 54 (67.5)	10 (38.5) 30 (55.6)	16 (61.5) 24 (44.4)	0.311
Histopathological type: Conventtosomal adenocarcinoma Mucoïd carcinoma	70(92) 10 (8)	38 (96) 4 (4)	32 (94) 6 (6)	0.49
Initial site: Ra Rb	16 (32.5) 64 (67.5)	9 (7) 31 (93)	7 (5) 33(95)	0.603
Grade: I II III	12 (15) 30 (37.5) 38 (47.5)	6 (50) 18 (60) 16 (42.1)	6 (50) 12 (40) 22 (57.9)	0.585
T stage: T2 T3 T4a T4b	8 (10) 18 (22.5) 26 (32.5) 28 (35)	4 (50) 8 (44.4) 14 (53.8) 14 (50)	4 (50) 10 (55.6) 12 (46.2) 14 (50)	0.979
N stage: N1 N2 N3	14 (17.5) 22 (27.5) 44 (55)	10 (71.4) 16 (72.7) 14 (31.8)	4 (28.6) 6 (27.3) 30 (68.2)	0.239
Clinical stage: II III	32 (40) 48 (60)	22(68.8) 18 (37.5)	10 (31.2) 30 (62.5)	0.643
Tumor distance from anal verge (cm)†	5.0 (3.0–8.0)	5.0 (4.0–6.0)	5.0 (3.0–7.0)	0.89

*p<0.05 is statistically significant **p≤0.001 is statistically highly significant

∞ Chi square test ‡Independent sample t test

Ra indicates tumor center located above the peritoneal reflection, Rb, tumor center located below the peritoneal reflection

Table 2. Comparison between Total Mesorectal Excision (TME) With Lateral Pelvic Lymph Node Dissection (LPLD) and Total Mesorectal Excision (TME) alone for Management of Locally Advanced Low Cancer Rectum regarding operative and postoperative findings

Variables	Surgical technique		p
	TME and LPLD	TME	
	N=40 (%)	N=40 (%)	
Type of surgery ·· Low anterior resection Abdominoperineal resection Hartmann's procedure	6 (50) 18 (60) 16 (42.1)	6 (50) 12 (40) 22 (57.9)	0.585
Operative time (min.)	360 (296–429)	254 (210–307)	<0.001
Blood loss (mL)	576 (352–900)	337 (170–566)	<0.001
Lateral lymph node metastasis	3 (8%)	----	0.49
Intraoperative bleeding	4 (10)	3 (8)	0.07
Intraoperative complications	2 (5)	2 (5)	1
Post-operative complications	2 (5)	2 (5)	1
Postoperative 30 days mortality	0 (0)	0(0)	1

*p<0.05 is statistically significant **p≤0.001 is statistically highly significant

∞ Chi square test ¥Independent sample t test

Table 3. Comparison between Total Mesorectal Excision (TME) With Lateral Pelvic Lymph Node Dissection (LPLD) and Total Mesorectal Excision (TME) alone for Management of Locally Advanced Low Cancer Rectum regarding response to treatment and patient outcome (relapse and death):

Variables	Surgical technique		p
	TME and LPLD	TME	
	N=40 (%)	N=40 (%)	
Anastomosis	1 (2.5)	1 (2.5)	0.008
Central pelvis	1 (2.5)	1 (2.5)	
Central and lateral pelvis	1 (2.5)	1 (2.5)	
Lateral pelvis	1 (2.5)	6 (15)	
Definite residual tumor	1 (2.5)	4 (10)	
Total (%)	5 (12.5)	13 (32.5)	
Relapse (n=18):			0.022
Absent	35 (87.5)	27 (67.5)	
Present	5 (12.5)	13 (32.5)	
Death			0.047*
No	37 (92.5)	42 (80)	
Yes	3 (7.5)	8 (20)	
Disease free survival:			0.027*
Median	26.5	25	
Range	18 - 32	15 - 30	
Overall survival:			0.001**
Median	19	8	
Range	7 - 23	6 - 15	

*p<0.05 is statistically significant **p≤0.001 is statistically highly significant

¥Mann Whitney test ∞ Chi square test

Discussion

In the current study we compared performing total mesorectal excision alone with performing it in addition to performing lateral lymph node dissection in patients with cancer rectum and we showed that although the technique of patients underwent total mesorectal excision and lateral pelvic lymph nodes dissection takes a longer time with slightly higher incidence of complication but it decreased incidence of local recurrence and improved patients survival than patients underwent total mesorectal excision only.

Wang et al., [11] found no differences between both technique regarding disease recurrence or survival rates.

Fujita et al., [12], showed that there is decreased recurrence and improved survival in the group operated by total mesorectal excision alone in addition to chemoradiotherapy.

Sugihara et al., [13] reported a significant reduction in pelvic recurrence after performing lateral lymph nodes dissection.

Previous studies showed the survival benefits of performing lateral lymph nodes dissection in addition to total mesorectal excision in cancer rectum management [14-17].

Other authors showed different results; that performing only total mesorectal excision decreased incidence of local recurrence and improved survival [18]

Additionally it was found that performing total mesorectal excision in addition to neoadjuvant chemo-radiotherapy might lead to reduction in the incidence of recurrence more than performing total mesorectal excision and lateral pelvic lymph nodes dissection [19].

total mesorectal excision and lateral lymph nodes dissection has slightly higher number of complications but without statistically significant differences similarly [11, 20].

Moreover, Cheng et al [21], found a longer time of operation, a larger amount of intra-operative blood loss, higher incidence of sexual and urinary dysfunction in cases of performing lateral lymph nodes dissection but incidence of perioperative mortalities, morbidities and long term oncological and survival outcomes were similar.

Japanese surgeons advised performing lateral pelvic lymph nodes dissection regarding improving survival and decreasing recurrence but western surgeons considered lateral pelvic lymph nodes dissection as a high-risk surgical procedure which has more complications [11]. Additionally it was found that using neoadjuvant

chemoradiotherapy has the benefits of reducing risk of local recurrence alternative to lymph nodes dissection with less surgical related complications [19]. Japanese surgeons suggested that there were higher possibilities of disease recurrence after neoadjuvant chemoradiotherapy, so performing lateral lymph nodes dissection could yield better results.

Taking all previous results in consideration and results of the present studies, it was found that benefits of performing lateral pelvic lymph nodes dissection in addition to total mesorectal excision are not yet clear regarding decreasing recurrence and improving survival of rectal cancer patients [4].

Conclusions

We concluded that performing lateral pelvic lymph nodes dissection in addition to total mesorectal excision although has slightly more complications that performing total mesorectal excision alone but could improve the survival of the patients and decreasing rate of local recurrence.

Recommendations

Further studies including larger number of patients are needed to prove our results and showed oncological benefits of performing lateral pelvic lymph nodes dissection.

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