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Predictive Factors of Difficulty during Laparoscopic Total Mesorectal Excision in Rectal Cancer

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ABSTRACT

Background: Despite the fact that laparoscopic resection is considered a standard technique in colon cancer, its role in rectal cancer is still under research. Total mesorectal excision allows en bloc removal of the mesorectum with the rectal fascia and decreases the recurrence rate to 5%. The aim of the study was to evaluate the factors predicting difficulty of the laparoscopic total mesorectal excision in anorectal cancer.
Patient and Methods: Twenty-four patients were included in the study. Laparoscopic total mesorectal excision was done in all patients. Gender, body massindex, tumor diameter, tumor distance from the anal verge, preoperative chemotherapy, and 5 pelvic dimensions (pelvic inlet, pelvic outlet, length of sacrum, interspinous distance, and intertuberous distance) were analyzed as variables affecting the difficulties of laparoscopic TME.
Results: Multivariate analysis showed that BMI (P<0.0001), tumor distance from the anal verge (P=0.0003), tumor depth (P=0.0021), and pelvic outlet (P=0.0362) were independently predictive of pelvic operative time. Pelvic operative time was related to intraoperative blood loss (P<0.0001). The tumor distance from the anal verge (P=0.0333, odds ratio 1.06) was related to postoperative morbidity, and pelvic outlet was related to anastomotic leakage (P=0.0305, OR: 1.13).
Conclusion: Higher BMI, shorter distance from anal verge and narrow pelvic outlet are predictive factors of longer operative time in laparoscopic TME.
Keywords: Mesorectal, Cancer, Laparoscopic, Anorectal.

INTRODUCTION

Total Mesorectal Excision (TME) is a standard oncologic procedure for low rectal cancerthat has been shown to decrease local recurrence.[1] Many studies have also shown that TME is a technicallydemandingprocedure thatrequires precisedissectionof themesorectum betweenthevisceralfasciaand thepelvic fascia in thenarrowspaceof thepelvic cavity.[1-4]Inparticular, laparoscopic rectalsurgery is technicallydifficult, and it requires advanced laparoscopic surgical skills.[5] An initial randomized controlled trial reported impaired short-term outcomes after laparoscopic anterior resection for rectal cancer,[6]although recent nonrandomized studies have suggestedthatlaparoscopic rectalsurgeryis safe and feasible.[7-12]

Thelaparoscopic approachoffersaclearand magnified image, but intracorporeal dissectionand transection of the rectum and anastomosis are difficult procedures of the laparoscopic TME.[5,13] In particular,intracorporeal rectaltransection following TME using commercially available devices have the limitations withinthehuman pelvis.[13]Therefore, animproved understandingofthepreoperative factorsassociatedwithdifficultiesoflaparoscopic TME with intracorporeal rectal transection and anastomosisis important forsurgeons. Recentstudies have suggested that the quality of TME is influenced notonlybythesurgeon’sskillsbutalsobythe patient’sclinicalandanatomical factors,suchas sex, tumor distancefrom the anal verge, andpelvic size in opensurgery.[14-17] However, few reports exist that evaluate the influence of such factors on

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difficulties in laparoscopic settings.[18]Thepurpose of this study was to evaluate the clinical and anatomical factors,particularly pelvic diameters, which influence the difficulties in laparoscopic TME.

PATIENTS AND METHODS

After approval of the University Ethical Committee, this study was conducted on patients presenting with mid and low rectal cancer to the outpatient clinic of both Zagazig University Hospitals & El-Salam Oncology Center during the period from July 2017 to 2020.All the procedures were done on elective basis.

Inclusion criteria included ages between 15-70 years and fitness for laparoscopic surgery. While patients with tumors above rectosigmoid junction, patients with locally advanced rectal cancer, patients with metastatic rectal cancer (except liver metastasis) and all emergency cases (e.g. perforation, obstruction) were excluded.

Thedatawere collected prospectivelyfor age, gender, body mass index(BMI),tumor size, tumor staging,duration of operation, amount of bloodloss, conversion to opensurgery, and postoperative data, including pathology, hospitalstay, 30-day morbidity, and mortality.Pathologic examination was carried out according tothe generalrulesoftheJapanese Society for Cancerof theColonandRectum.[19]

Pretreatment clinicalstagingwas performed by usinga combination of physicalexamination, colonoscopy,andabdominal computed tomography (CT).

The outcomes of interest were pelvic operative time, which was defined as the time required for the dissection of the rectum from the pelvis, intracorporeal transaction, andanastomosis. The operative timewas calculated as thetimefromthestartof dorsaldissectionof therectum untiltheendof pneumoperitoneum by checkingthevideo record. Other outcomes of interest were intraoperative bloodloss, overall postoperative morbidity,andanastomotic leakage. Anastomoticleakagewas diagnosed by the presenceofanyofthe following:gasorfecal discharge fromtheincisionalwound,vagina,or draintract; fecal peritonitis; or intra-abdominal abscessorperitonitis alongwithananastomotic defect verified byimage study.Intraperitoneal abscess neartheanastomotic site withoutan obviousfecalfistulawas alsodiagnosed as aclinical leakage.Thepelvic operativetimeandintraoperative bloodloss were evaluatedas a continuous variable. Characteristics evaluatedas categoricalvariablesincluded gender(male andfemale),and preoperativechemotherapy. The characteristics evaluatedas continuous variables included BMI, tumor size, tumor distance fromtheanalverge,and5 pelvic dimensions; The pelvic inlet (alinefromthe superior aspect of the pubic symphysis to the sacral promontory), pelvic outlet(alinefromtheinferioraspectof thepubicsymphysis to thecoccyx), and lengthof sacrum(the distancefrom the sacral promontorytothecoccyx)weremeasured on lateralCT scout images. The interspinous distance (thenarrowestdistancebetweenthe ischial spines) andtheintertuberous distance(thedistance between thelowest aspectof theischial tuberosities) were measured on axial CT images. The CT scout imageswere viewed inconjunction with axial CT imagesusingoptimized window settingsindividualized for eachpatient.

STATISTICAL ANALYSIS

Analysis was performed using the Fisher exact test, Mann-Whitney U test, or Spearman rank correlation coefficient when appropriate. After univariateanalysis, variables with a P value less than0.25 were selectedfor multivariate analysis. A multivariate analysis was performed using a multiple linear regression model with a stepwise (forward selection/backward elimination) method

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(significance level to enter = 0.25, significance level to stay = 0.1). The overallpostoperativemorbidityandanastomoticleakagewereevaluatedwitha multivariate logisticregression analysis. P value less than0.05 was considered to be significant.

RESULTS

Thepatientandtumorbackgroundsofthe24 patients included in thestudy aresummarized inTable1.Themeanagewas 52years(range,35-75),and8patients(33.3%)weremale.The meanBMIwas23.6kg/m^2(range, 15.4-35.2). Themeantumor distancefromtheanalverge was 5.7cm. Twenty patients receivedneoadjuvant chemotherapy(either short or long course). Twenty-three patientshadadenocarcinoma (mainly grade II) and1 patient hadGIST.

Pelvic dimensions aresummarized inTable2. All of the pelvic dimensions were statistically differentbetweenmales andfemales.Overall, male pelvisesweredeeperandnarrowerthanfemale pelvises,asshownpreviously.Theintraoperative andpostoperativeoutcomesaresummarized in Table3.Themeanpelvicoperativetimewas153min(range,89-395),andthemeanblood loss was 17 mL (range, 0-220). A divertingileostomy was created in 12 patients. No positivelongitudinal or circumferential resection margins were identified. Therewas noconversiontoopensurgery orhospitaldeaths.

Thecorrelations betweenpelvic operativetime andclinicoanatomical factorsaresummarized inTable 4. A univariate analysis showed thatgender,tumor distancefromtheanalverge, pelvic outlet, interspinous distance,andintertuberousdistanceweresignificantlyassociatedwithpelvicoperativetime.A stepwiselinearregressionanalysisshowedthattheoptimal modelto predict thepelvic operativetimeincluded BMI, tumor distancefromtheanal verge, andpelvic outlet(P <0.0001, Table 5). The results of multivariate analysis for intraoperative bloodloss, overall postoperative morbidity,andanastomotic leakagearesummarized inTable6.Thepredictorsforintraoperative bloodloss were pelvic operative time(P <0.0001). Thepredictors for overall postoperative morbidity weretumordistancefromtheanalverge(P=0.0333, oddsratio[OR]:1.06, confidence interval [CI]95%: 1.00--1.12), andthepredictors for anastomoticleakagewere pelvic outlet(P = 0.0305, OR:1.13, CI 95%: 1.01--1.29).

Table (1): Patient and tumor background

Gender (male/female)	8/16
Mean age *(yrs)*	52.2±12.4 (35-75)
Mean BMI *(Kg/m^2)*	23.6 (15.4-35.2)
Mean tumor size *(mm)*	34 (7-70)
Mean tumor distance from anal verge *(cm)*	5.75±4.96 (1-15)
Neoadjuvant Chemotherapy	20 (83.4%)
Tumor Pathology	
– Adenocarcinoma	23 (95.84%)
– GIST	1 (4.16%)
Tumor Grade	
– I	2 (8.3%)
– II	20 (83.3%)
– III	2 (8.3%)

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Table (2): Pelvic dimensions

	Overall (n=24)	Male (n=8)	Female (n=16)	P Value
Mean Pelvic inlet *(mm)*	122 (101-150)	117 (101-135)	127 (102-150)	**0.0003**
Mean Pelvic outlet *(mm)*	98 (79-122)	94 (79-111)	103 (87-122)	**<0.0001**
Mean Sacral length *(mm)*	130 (104-159)	133 (104-159)	126 (108-142)	**0.0082**
Mean interspinous distance *(mm)*	99 (80-126)	92 (80-105)	109 (91-126)	**<0.0001**
Mean intertuberous distance *(mm)*	116 (93-148)	108 (93-131)	126 (103-148)	**<0.0001**

Table (3): Intraoperative and postoperative outcomes

Mean operative time *(min)*	150.4±32.6 (120-210)
Mean blood loss *(ml)*	181.8±48.97 (100-250)
Temporary diversion *(ileostomy)*	12 (50%)
Conversion	0 (0%)
Mean number of harvested LN	10.7±4.5 (6-24)
Free Surgical Margin	24 (100%)
Complications	
– No	20 (83.3%)
– Wound infection	1 (4.16%)
– Stoma complication	1 (4.16%)
– Chest infection	1 (4.16%)
– Leakage	1 (4.16%)
Mean Hospital stay *(days)*	2.6±0.69 (2-4)

Table (4): Correlation between operative time and clinicoanatomic factors

Variable	P Value
Gender	0.0034
BMI	0.077
Tumor size	0.419
Tumor Distance	0.0004
Neoadjuvant chemotherapy	0.0109
Pelvic Inlet	0.1158
Pelvic outlet	0.0345
Sacral length	0.9986
Interspinous distance	0.0063
Intertuberous Distance	0.0044

Table (5): Stepwise linear regression analysis for operative time

Variable	Estimate	P Value
Intercept	5.37	<0.0001
Body Mass index	0.0305	<0.0001
Tumor distance	-0.0072	0.0003
Pelvic outlet	-0.0064	0.0362

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Table (6): Multivariate analysis for other factors

Dependent	Predictive	P value	Odds ratio	95% CI
Blood loss	Operative time	<0.0001		
Overall morbidity	Tumor distance	0.0333	1.06	1.00-1.12
Leakage	Pelvic outlet	0.0305	1.13	1.01-1.29

DISCUSSION

Although laparoscopic colorectal resection is well established for colonicandupper rectalcancers,severaltechnicallimitationsareassociated with resection of middleandlow rectalcancers.[6,7]

Division of the rectum after TME using intracorporeal staplingdevices is technicallydifficult because of theirwidth andlimitedreticulation.[13]Previous studieshavereported thatfactorssuchasmale gender,shortertumordistancefromtheanal verge, andnarrower pelvic dimensions areassociatedwith poorer outcomes of openrectalsurgery, especiallyinrelation toanastomotic leakageand circumferential resectionmargin.[15-17,20]Thisreportis thefirst toevaluatetheinfluence of such factorsonthedifficultiesoflaparoscopicTME with intracorporeal rectaltransection andanastomosis for low rectalcancer.

Inthecurrent study, we evaluatedcases of low rectalcancerthatunderwentlaparoscopicTME with DST anastomosis, becauseintracorporealrectal transection andanastomosis is oneof themost difficultproceduresoflaparoscopicTMEand should be evaluated separately from cases that underwent abdominoperineal resection, intersphincteric resection, anda prolapse method for rectaltransection. Furthermore, we selectedoperative time after the start ofdissectionof the rectum fromthepelvis as a dependent variable associated with technical difficultiesof laparoscopic TME for the following reasons.First, we could minimizetheinfluence of abdominal adhesions, which wouldincrease the operative time before achieving therectal dissection from the pelvis. Second, pelvicdimensions would influence the procedures moredirectly after reaching the pelvic cavity. Third, theprocedures in the pelvis were performed by a wellexperienced surgeon in all cases, but the procedures before the rectal dissection (retroperitonealdissection of the sigmoid mesocolon, division ofthe inferior mesenteric vessels, and lateral dissection of the sigmoid mesocolon) were performed bysurgical trainees in our institution in some cases,which would cause intersurgeon bias. Thus, byexcluding the procedures outside the pelvis, wecould analyze the factors that affected dissection,rectal transection, and anastomosis in the pelvismore accurately.

In the current study, a multivariate analysisshowed that higher BMI, shorter tumor distance from the anal verge, advanced tumor depth, andnarrower pelvic outlet were significantly associated with longer operative time. Furthermore, longeroperative time was significantly associated with more intraoperative blood loss. The tumor diameter was not related to operative time in thecurrent study, because tumor diameter may notcorrelate well with tumor volume. In open TME, shorter tumor distance from the anal verge isthought to be a major factor that elongates operative time.[15]Similarly with open TME, our datademonstrate for the first time that shorter tumor distance from the anal verge is a risk factor for longer operative time in laparoscopic TME with intracorporeal rectal transection and anastomosis.The range of our BMI data was 15.4-35.2 kg/ m^2, which is lower than in Western populations.

Nonetheless, higher BMI was also predictive of longer operative time. However, the potential disadvantage of BMI is that the value does notconsistently reflect body adipose tissue accumulation. On the one hand, the multivariate analysisin the male subgroup showed that only BMI was predictive of operative time. On the other hand,the multivariate analysis in the female subgroup did not identify BMI as a predictive factor of operative time. Considering body fat distribution

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(visceral fat or abdominal subcutaneous fat) may benecessary to predict more accurately longer operative time.
In the current study, narrower pelvic outlet wassignificantly associated with longer operative time. A recent study reported that narrow pelvic inletand shorter interspinous distance were significantly associated with poor postoperative specimenquality in open TME.[16]Our data are comparable with a previous report showing that male genderand narrower pelvic outlet are independent predictive factors for longer operative time of laparoscopic rectal surgery involving high or low anterior resection and abdominoperineal resection.[18]Importantly, we showed for the first time that narrower pelvic outlet was associated with longer operative time in laparoscopic TME.
Here, we could identify the predictive factor ofoverall postoperative morbidity and anastomotic leakage. The independent predictive factor foroverall postoperative morbidity was longer tumor distance from the anal verge, and the independentpredictive factor for anastomotic leakage was larger pelvic outlet. Unexpectedly, a univariateanalysis showed that shorter pelvic operative time was associated with anastomotic leakage, althoughthe value was not statistically significant (P=0.0781). Analyzing the predictive factor of conversion toopen surgery was impossible in the current studybecause there were no conversion to open surgery.A positive circumferential resection margin occurredin 1 male patient who had an advanced tumor(T3N2) with BMI 35.2 kg/m^2.The limitation of this study to be noted is therelatively small number of patients who underwentpreoperative chemotherapy therapy. This mightbe why preoperative chemotherapy therapy wasnot a significant predictive factor of operative timein this study. In our institution, the indications ofpreoperative chemotherapy were T3/T4tumors staged by magnetic resonance imagingand/or node-positive tumors below the peritonealreflection, but preoperative chemotherapy was tended to be selected to the patients withlow locally advanced tumors to increase the chance ofsphincter-preserving operation. For this reason,8 laparoscopic intersphincteric resections and6 laparoscopic abdominoperineal resections wereperformed for the patients who underwent preoperative chemotherapy therapy during the sameperiod. However, we previously reported that laparoscopic TME after chemotherapy therapy is asafe procedure with reasonable operative time.[21]

CONCLUSION

Higher BMI, shorter tumor distance from the anal verge, advanced tumor depth, and narrower pelvic outlet were independentlypredictive of longer operative time in laparoscopic TME. To perform laparoscopic TMEsafely, these factors should be taken into accountbefore operation.

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