



## **The Value of Tumor Size as a Prognostic Factor in Rectal Adenocarcinoma**

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### **Authors' contributions**

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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## **ABSTRACT**

**Background:** Colorectal cancer (CRC) is the third frequent diagnosed cancer and third cause of cancer death. Curative intent surgery followed by chemoradiotherapy are the standard of care for patients with CRC to reduce local recurrence and enhance overall survival (OS). This study aimed to evaluate tumor size as a prognostic factor for rectal adenocarcinoma local recurrence.

**Patients and Methods:** This retrospective phase II study reviewed 100 rectal adenocarcinoma patients who were treated and followed up for 5 years after treatment. The medical records were reviewed for all cases including demographic data, medical history, personal habits, uncontrolled chronic medical condition, presenting symptoms and signs, pathological data, laboratory investigations, diagnosis, radiological examination, treatment details and treatment outcome assessed by OS and disease-free survival (DFS).

**Results:** During 5 years of follow up in our study, 12 patients (12%) had local recurrence. Patients with tumor size > 5 cm has a significantly shorter DFS. DFS within 2-yrs for tumours ≤5 cm 96%, while 5-years DFS was 90%. While for tumours >5cm, 2-years DFS was 70% and 55% for 5-years and more. In tumours size >5cm, 2-years OS was 75%, 3-years OS was 72% and 5-years was 70% While In tumours ≤ 5cm, overall survival was 84%. Patients who had neoadjuvant chemoradiation also had a significant low local recurrent rate with (p=.042) in multivariate analysis.

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**Conclusions:** Tumor size has a prognostic value in rectal adenocarcinoma. Tumor size >5 cm is associated with higher rate of local recurrence and worse DFS.

*Keywords:* Tumor size; prognosis; survival; rectal adenocarcinoma; recurrence.

## 1. INTRODUCTION

Colorectal cancer (CRC) is the third most frequently diagnosed cancer and the third leading cause of cancer death in the USA. In 2020, an estimated 43,340 new cases of rectal cancer were diagnosed in the USA: 25,960 men and 17,380 women. During the same year, it was estimated that 53,200 people would die from rectal and colon cancer combined [1].

Most rectal tumours are carcinomas. Of the carcinomas, >90%) are adenocarcinomas [2].

Surgical resection is the primary treatment modality for CRC. However, although colon and rectal cancers share many features, some crucial differences are present between these two cancers, which include the tendency of rectal cancer to recur locally [3].

Local recurrence of rectal cancer is common (15%)–45%) after a standard surgery and is often catastrophic. Moreover, local recurrence is difficult to cure, and the associated symptoms are debilitating. Therefore, preventing or predicting local recurrence is one of the main goals in rectal cancer treatment [4].

Until now, the most powerful method for assessing prognosis following a potentially curative surgery for CRC is the pathological analysis of the resected specimen. Other clinical and histological features may influence the prognosis regardless of the stage [5].

The actual prognostic factors of local recurrence in rectal adenocarcinoma following a surgery cannot be adequately extrapolated. The assessment of prognosis in patients with rectal adenocarcinoma is crucial with respect to surveillance and selection of neo-adjuvant or adjuvant therapy [6].

Therefore, this study investigated the value of tumor size as a prognostic factor for local recurrence in patients with rectal adenocarcinoma.

## 2. PATIENTS AND METHODS

This retrospective phase II study included a review of 100 patients with rectal

adenocarcinoma presented to Tanta Clinical Oncology Department and Meet Ghmmr Oncology Center (1:1) during the period from January 2015 to December 2017 inclusive and 5 years follow-up.

Eligibility criteria were histologically confirmed diagnosis of primary adenocarcinoma of the rectum, age > 18 years, patients had curative surgery, received systemic therapy as recommended by guidelines and stage I-III rectal cancer.

Exclusion criteria were the presence of metastatic rectal cancer, palliative intent treatment. Histological diagnoses as non-adenocarcinoma rectal cancer, inflammatory bowel disease and previous pelvic radiotherapy.

We reviewed the medical records of all patients including demographic data, medical history, personal habits, uncontrolled chronic medical condition (hypertension, diabetes mellitus and past history of previous surgery), presenting symptoms and signs (bleeding per rectum, change in bowel habit or weight loss, intestinal obstruction and perineal pain), pathological data (histopathology, tumor size and extension, the status of lymphovascular or perineural invasion, surgical margins and circumferential resection margin (CRM), number of lymph nodes harvested and positive lymph nodes and tumour, node and metastasis (TNM) staging), laboratory investigations (CBC, kidney and liver profile, CEA and CA19.9), diagnosis (proctoscopic examination and transanal biopsy), radiological examination (MRI of abdomen and pelvis, Post-contrast CT chest, PET-CT scan and bone scan).

### 2.1 Treatment Details

**Surgery:** Total mesenteric excision (TME); Low anterior resection (LAR) or Abdomino-perineal resection (APR).

**Chemo-radiotherapy** (dose and time; neo-adjuvant or adjuvant). Patients received radiotherapy dose of 45Gy/25 fractions over 5 weeks concomitant with capecitabine 825mg/m<sup>2</sup> BID daily with radiotherapy.

**Chemotherapy:** Protocol and number of cycles and timing (FOLFOX (oxaliplatin + leucovorin +

5-fluorouracil) /XELOX (capecitabine plus oxaliplatin), biweekly for 4 months) as neoadjuvant or adjuvant.

### 2.2 Treatment Outcome (Survival Details) Assessed by

**Overall survival:** Calculated in months elapsing between date of diagnosis and date of death or last visit.

**Disease-free survival:** Calculated in months elapsing between radical surgery and detection of recurrence either at surgical bed or at distant site.

### 2.3 Statistical Analysis

Data were fed to the computer and analyzed using IBM SPSS software package version 26.0. (Armonk, NY: IBM Corp). Numerical data was expressed as median, mean, or standard deviation. While quantitative data was expressed as frequency and percentage. Significance of the obtained results was considered at 0.05.

## 3. RESULTS

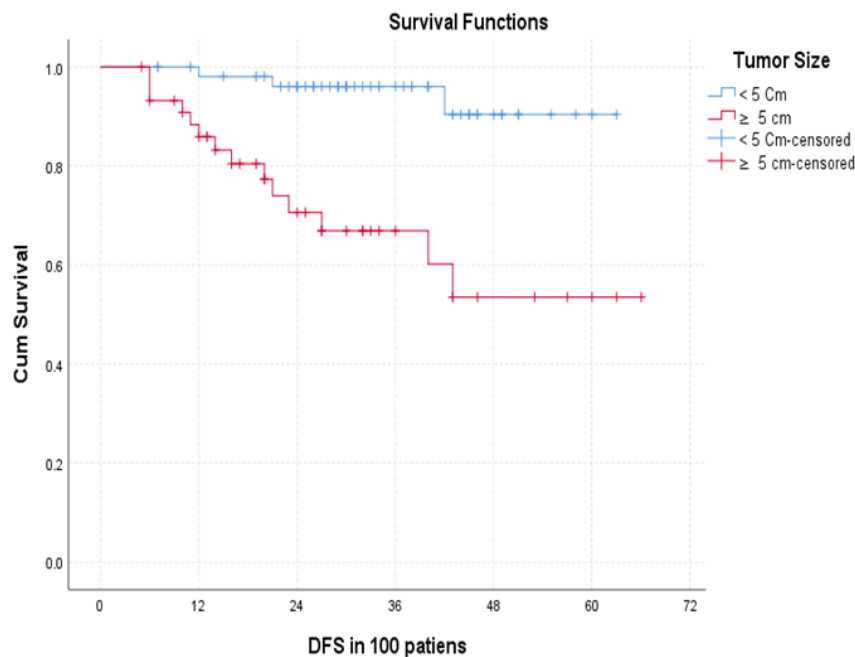
The present study included 100 patients who diagnosed with rectal adenocarcinoma and underwent a radical surgery with the following characteristics.

The correlation between clinicopathological factors and local recurrence showed that local recurrence was significantly associated with young patient (<50years) ( $p=.011$ ), large tumor size (>5cm), locally advanced stage III, positive lymph nodes involvement and positive involvement of CRM with ( $p=0.011$ ), ( $p=0.008$ ), ( $p=0.010$ ), ( $p=0.002$ ) and ( $p=0.003$ ), respectively.

The correlation between clinicopathological factors and tumor size showed that tumor >5 cm tends to be locally advanced stage III ( $p=.009$ ) with more tumor depth invasion (T stage) ( $p=.047$ ) and positive lymph node metastasis ( $p=.006$ ).

A univariate COX regression analysis showed that there are multiple factors affecting time to local recurrence including large tumor size ( $p=.015$ ), locally advanced stage III ( $p=.013$ ), positive nodal stage ( $p=.012$ ), positivity of CRM ( $p<.001$ ). Receiving radiotherapy was significant whenever the timing. For adjuvant CCRT ( $p=.024$ ) and ( $p=.008$ ) for neoadjuvant CCRT.

A multivariate COX regression analysis showed that tumor size >5 cm had a high incidence of recurrence. So, tumor size has a statistically significance in prediction of the probability of tumor recurrence ( $p=.038$ ). Neoadjuvant concomitant chemoradiation also shows significance in local recurrence ( $p=.042$ ).



**Fig. 1. Kaplan-meier curve of disease-free survival according to tumor size in the studied patients (total n=100)**

**Table 1. Patients' and tumor characteristics in studied patients**

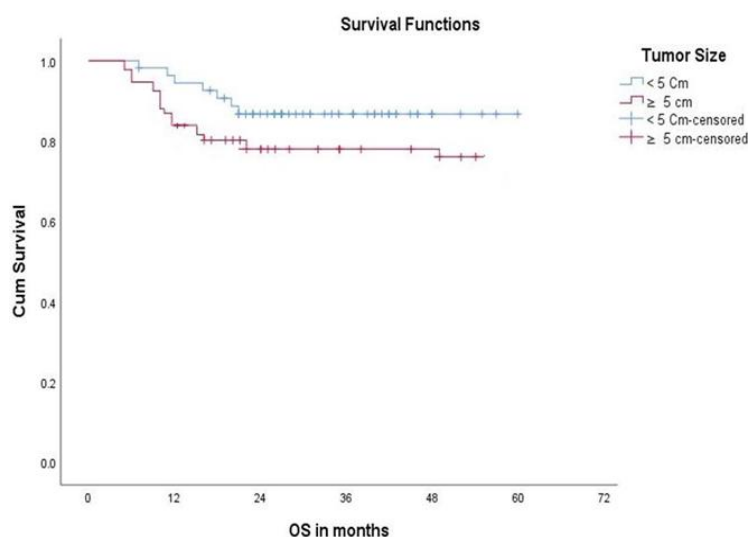
		<b>Number (%)</b>
<b>Gender</b>	Male	55 (55%)
	Female	45 (45%)
<b>Age</b>	< 50 years	34 (34%)
	≥ 50 years	66 (66%)
	Mean	53.59 (19-79 years)
<b>Surgery type</b>	APR	42 (42%)
	LAR	52 (52%)
	Intersphincteric	6 (6%)
<b>Tumor size</b>	< 5 cm	67 (67%)
	≥ 5 cm	33 (33%)
	Mean	4.976 (2-10 cm)
<b>Site in rectum</b>	Upper third	17(17%)
	Upper middle	18(18%)
	Middle third	20(20%)
	Middle-lower	19(19%)
	Lower third	26(26%)
<b>Stage</b>	Stage I	17(17%)
	Stage II	33(33%)
	Stage III	50(50%)
<b>Grade</b>	Well differentiated	15(15%)
	Mod-differentiated	63(63%)
	Poorly differentiated	22(22%)
<b>T stage</b>	T1	1(1%)
	T2	27(27%)
	T3	60(60%)
	T4	12(12%)
<b>N stage</b>	N0	50(50%)
	N1	32(32%)
	N2	18(18%)
<b>CRM</b>	Positive	11(11%)
	Negative	89(89%)
<b>LVI</b>	Positive	12(12%)
	Negative	88(88%)
<b>Chemotherapy</b>	No chemotherapy	21(21%)
	Adjuvant	41(41%)
	Neo-adjuvant	38(38%)
<b>Chemoradiotherapy</b>	No	8(8%)
	Adjuvant	41(41%)
	Neo-adjuvant	51(51%)
<b>All Rec. during follow-up</b>	Positive	17(17%)
	Negative	83(83%)
<b>All Met. During follow up</b>	Positive	22 (22%)
	Negative	78 (78%)
<b>Both Mets and recurrence</b>	Both rec and mets	5(5%)
	Only local recurrence	12(12%)
	Only distant mets	17(17%)
<b>Fate</b>	Dead	28(28%)
	Alive	72(72%)

Data were presented as frequency (%). Mets: metastatic, CRM: circumferential resection margin, LVI: Lymphovascular invasion, Rec: Recurrence, APR: Abdomino-perineal resection, LAR: Low anterior resection and CCRTH: concurrent chemoradiotherapy

**Table 2. Correlation between clinicopathological factors and local recurrence**

		+Ve recurrence %	-Ve recurrence %	P
<b>Gender</b>	Male(n=55)	8(14.5%)	47(85.5%)	.387
	Female (n=45)	4(8.9%)	41(91.1%)	
<b>Age</b>	<50 yrs (n=34)	8(23.5%)	26(76.5%)	.011*
	≥50 yrs (n=66)	4(6.1%)	62(93.9%)	
<b>Surgery type</b>	APR (n=42)	6(14.3%)	36(85.7%)	.549
	non-APR (n=58)	6(10.3%)	52(89.7%)	
<b>Tumor size</b>	≤ 5 cm (n=67)	4(7.1%)	52(92.9%)	.008*
	> 5 cm (n=33)	8(18.2%)	36(81.8%)	
<b>Site (mainly)</b>	Upper (n=31)	4(12.9%)	27(87.1%)	.680
	Middle (n=27)	2(7.4%)	25(92.6%)	
	Lower (n=42)	6(14.3%)	36(85.7%)	
<b>Stage</b>	Stage I (n=17)	0(0.0%)	17(100%)	.010*
	Stage II (n=33)	2(6.1%)	31(93.9%)	
	Stage III (n=50)	10(20.0%)	40(80.0%)	
<b>Grade</b>	Well-diff(n=15)	1(6.7%)	14(93.3%)	.205
	Mod-diff(n=63)	6(9.5%)	57(90.5%)	
	Poor-diff(n=22)	5(22.7%)	17(77.3%)	
<b>T stage</b>	T1-3 (n=88)	10(11.4%)	78(88.6%)	.596
	T4 (n=12)	2(16.7%)	10(83.3%)	
<b>N stage</b>	N0 (n=50)	1(2.0%)	49(98.0%)	.002*
	N1-2 (n=50)	11(22.0%)	39(78.0%)	
<b>CRM</b>	Positive (n=11)	7(97.9%)	82(92.1%)	.003*
	Negative (n=89)	5(45.5%)	6(54.5%)	
<b>LVI</b>	Positive (n=12)	10(11.4%)	10(83.3%)	.596
	Negative (n=88)	2(16.7%)	78(88.9%)	
<b>Adjuvant Chemotherapy</b>	No (n=59)	5(8.5%)	54(91.5%)	.193
	Yes (n=41)	7(17.1%)	34(82.9%)	
<b>CCRTH</b>	Neo-adj (n=51)	3(5.8%)	48(94.2%)	.047*
	Adj (n=41)	7(17.1%)	34(82.9%)	
	No (n=8)	2(25%)	6(87.5%)	

Data were presented as frequency (%). \*: Statistically significant at  $p \leq 0.05$ . Mets: metastatic, CRM: circumferential resection margin, LVI: Lymphovascular invasion, Rec: Recurrence, APR: Abdomino-perineal resection, LAR: Low anterior resection and CCRTH: concurrent chemoradiotherapy



**Fig. 2. Kaplan-meier curve of overall survival according to tumor size in the studied patients (total n=100)**

**Table 3. Correlation between clinicopathological factors and tumor size**

		<5cm (%)	>5cm (%)	P value
<b>Gender</b>	Male(n=55)	37(67.3%)	18(32.7%)	.949
	Female (n=45)	30(66.7%)	15(33.3%)	
<b>Age</b>	< 50 yrs (n=34)	23(67.6%)	11(32.4%)	.921
	≥50 yrs (n=66)	44(66.7%)	22(33.3%)	
<b>Surgery type</b>	APR (n=42)	25(59.5%)	17(40.5%)	.176
	Non-APR (n=58)	42(72.4%)	16(27.6%)	
<b>Tumor size</b>	≤ 5 cm (n=67)	4(7.1%)	52(92.9%)	.168
	> 5 cm (n=33)	8(18.2%)	36(81.8%)	
<b>Site (mainly)</b>	Upper (n=31)	17(54.8%)	14(45.2%)	.168
	Middle (n=27)	21(77.8%)	6(22.2%)	
	Lower (n=42)	29(69%)	13(31.0%)	
<b>Stage</b>	Stage I (n=17)	16(94.1%)	1(5.9%)	.009*
	Stage II (n=33)	23(69.6%)	10(30.4%)	
	Stage III (n=50)	28(36.6%)	22(45.1%)	
<b>Grade</b>	Well-diff (n=15)	11(73.3%)	4(26.7%)	.824
	Mod-diff (n=63)	42(66.7%)	21(33.3%)	
	Poorly diff(n=22)	14(63.3%)	8(36.4%)	
<b>T stage</b>	T1-3 (n=88)	62(70.5%)	26(29.5%)	.047*
	T4 (n=12)	5(41.7%)	7(58.3%)	
<b>N stage</b>	N0 (n=50)	40(80.0%)	10(20.0%)	.006*
	N1-2 (n=50)	27(54.0%)	23(46.0%)	
<b>CRM</b>	Positive (n=11)	5(45.5%)	6(54.5%)	.107
	Negative (n=89)	62(69.7%)	27(30.3%)	
<b>LVI</b>	Positive (n=12)	6(50%)	6(50%)	.182
	Negative (n=88)	61(69.3%)	27(30.7%)	
<b>Adjuvant chemotherapy</b>	No (n=59)	38(64.4%)	21(35.6%)	.508
	Yes (n=41)	29(70.7%)	12(29.3%)	
<b>CCRTH</b>	Neo-adj (n=51)	28(54.9%)	23(45.1%)	0.132
	Adj (n=41)	20(48.8%)	21(51.2%)	
	No (n=8)	7(87.5%)	1(12.5%)	

Data were presented as frequency (%). \*: Statistically significant at  $p \leq 0.05$ . Mets: metastatic, CRM: Circumferential Resection Margin, LVI: Lymphovascular invasion, Rec: Recurrence, APR: Abdomino-Perineal Resection, LAR: Low Anterior Resection and CCRTH: concurrent chemoradiotherapy

**Table 4. Univariate cox regression analysis of local recurrence rate in patients with rectal adenocarcinoma**

Comparison		Wald	P value
Age: < 50 yrs (n=34)	Vs ≥ 50 yrs (n=66)	4.867	.036*
Gender: Male (n=55)	Vs Female (n=45)	.626	.429
Surgery type: APR (n=42)	Vs Non-APR (n=58)	.467	.494
Tumor size: ≤ 5cm (n=67)	Vs >5cm (n=33)	5.949	.015*
Site in Rectum: Upper-middle (n=58)	Vs Lower third (n=42)	.371	.542
Stage I-II (n=50)	Vs Stage III (n=50)	6.122	.013*
Grade I, II (n=78)	Vs Grade III (n=22)	3.715	.054
T stage: T1-3 (n=88)	Vs T4 (n=12)	.631	.001*
N stage: N0 (n=50)	Vs N1-2 (n=50)	6.356	.012*
CRM: Negative (n=89)	Vs Positive (n=11)	13.082	<.001*
LVI: Negative (n=88)	Vs Positive (n=12)	.721	.396
Adjuvant CTH: Yes (n=41)	Vs No (n=59)	1.377	.241
CCRTH: Adjuvant (n=41)	Vs No	1.029	.024*
NA-CCRTH (n=51)	Vs (n=8)	1.045	.008*

\*: Statistically significant at  $p \leq 0.05$ . Mets: metastatic, CRM: Circumferential Resection Margin, LVI: Lymphovascular invasion, Rec: Recurrence, APR: Abdomino-Perineal Resection, LAR: Low Anterior Resection and CCRTH: concurrent chemoradiotherapy

**Table 5. Multivariate COX regression analysis of risk factors of recurrence in rectal cancer**

Comparison		Wald	P value
Age: < 50 yrs (n=34)	Vs ≥ 50 yrs (n=66)	1.129	.288
Gender: Male (n=55)	Vs Female (n=45)	.002	.962
Surgery type: APR (n=42)	Vs Non-APR (n=58)	2.523	.112
Tumor size: ≤ 5cm (n=67)	Vs >5cm (n=33)	2.986	.038*
Site in Rectum: Upper-middle (n=58)	Vs Lower third (n=42)	.224	.636
Stage I-II (n=50)	Vs Stage III (n=50)	.753	.386
Grade: well, mod (n=78)	Vs Poorly-diff (n=22)	3.007	.083
T stage: T1-3 (n=88)	Vs T4 (n=12)	.774	.379
N stage: N0 (n=50)	Vs N1-2 (n=50)	.515	.473
CRM: Negative (n=89)	Vs Positive (n=11)	2.834	.092
LVI: Negative (n=88)	Vs Positive (n=12)	.052	.819
Adjuvant chemotherapy: No adjuvant (n=41)	Vs Adjuvant (n=59)	.057	.811
CCRTH: Adjuvant (n=41)	Vs No	1.112	.058
Neoadjuvant (n=51)	Vs No	.917	.042*

\*: Statistically significant at  $p \leq 0.05$ . Mets: metastatic, CRM: Circumferential Resection Margin, LVI:

Lymphovascular invasion, Rec: Recurrence, APR: Abdomino-Perineal Resection, LAR: Low Anterior Resection and CCRTH: concurrent chemoradiotherapy

Disease free survival (DFS) was significantly shorter in patients with tumor size  $\geq 5$  cm ( $p=.007$ ). For tumor  $\leq 5$  cm DFS within 2-yrs 96%, while 5-years DFS was 90%. While for tumor  $>5$ cm, 2-years DFS was 70% and 55% for 5-years and more.

There was no difference in 5 years survival between patients who had tumor  $< 5$  cm and those who had tumor  $\geq 5$ cm, ( $p=0.195$ ). In tumours size  $\geq 5$ cm, 2 years overall survival (OS) was 75% and 5-years was 70%. While In tumours  $< 5$ cm, OS was 84% and 5-years OS was 76%.

#### 4. DISCUSSION

In our study, there was a significant correlation between local recurrence and tumor size and neoadjuvant chemoradiation. Our 5 years incidence of local recurrence matched with the study of Metwally et al. [7] that included 245 patients who registered at the Oncology Center, Mansoura University (OCMU) from 2006 to 2017, local recurrence incidence was 15.8%.

The incidence of rectal adenocarcinoma in our patients was higher in males (55) than female (45), with male to female ratio about 1.22 to 1. This had agreement with western countries, the male: female ratio was 1.33 to 1 in a study by Ansa et al. [8] and 1.24 to 1 in a study by White et al. [9].

In our study, gender had no predictive value of tumor recurrence with ( $p=.962$ ) in multivariate analysis, which is similar to Ogura et al. [10]

study in which 1216 patients with rectal cancer were included ( $p=.115$ ) and Zare-Bandamiri et al. [11] who included 561 patients with male: female ratio 1.35:1 and ( $p=.946$ ).

We found that age has no significant value for local recurrence in multivariate regression analysis ( $p=.288$ ). This result was similar to Dinaux et al. [12] study in which patients younger than 50 years had non-significant higher local recurrence due to late diagnosis in a multivariate regression analysis ( $p=.346$ ).

But our result was against Luo et al. [13] study, in which age was a significant factor especially for early local recurrence (within 2 years). Patients younger than 60 years had a higher local recurrence rate ( $p<.001$ ). This could be because in Luo et al. [13] study, patients did not receive neoadjuvant therapy.

In our study, tumor size was a significant prognostic factor for local recurrence. We found that tumor size  $\geq 5$ cm has a significant prognostic value of local recurrence ( $p=.004^*$ ) in a univariate analysis and ( $p=.048^*$ ) in a multivariate analysis.

This has agreement with Chen et al. [6] who enrolled 221 patients with rectal adenocarcinoma and had a significant value for local recurrence with ( $p=.013$ ).

In contrast, a study by Zare-Bandamiri et al. [11] showed that tumor size  $\geq 5$ cm in both colon and rectal cancer has no significant value on local recurrence in their 561 patients ( $p=.360$ ).

In our study, patients who received neoadjuvant chemoradiation showed significant low local recurrence rate. The study by Haggstrom et al. [14] showed that receiving radiotherapy whether adjuvant or neoadjuvant had a significant value only in univariate analysis ( $p=0.004$ ), but not in multivariate analysis ( $p=0.85$ ). This could be because only 44.7% of the 483 patients included received radiotherapy (36.9% as neoadjuvant and 7.8% as adjuvant) although 71.9% of the patients included were stage II and III.

In our study, APR surgery was higher in patients with tumor size more  $\geq 5$ cm. This was also in agree with a study compared between the APR and LAR procedures by Yeom et al. [15] which showed that there is no increase in local recurrence risk between APR and LAR in their 409 patients with ( $p=.724$ ).

On the other hand, when Nahas et al. [16] compared between the two types of surgery on a study included 148 patients with low rectal cancer (58.1% had APR and 41.9% had LAR in the period between 2002 to 2012, Nahas et al. [16] found that APR was associated with higher local recurrence ( $p=.009$ ) and worse 5-years OS. In Nahas et al. [16] study, APR was associated with more advanced (T3-T4, N+ve, poorly differentiated, +ve CRM) tumours.

In our study, half of the patients was locally advanced stage III (50%). Tumor stage was not a significant factor for local recurrence in multivariate analysis ( $p= .386$ ). This was similar to Denost et al. [17] study, which included 100 patients (the majority 66%) was stage III) and found no significant value of pathological stage or lymph nodes (LNs) status on local recurrence with ( $p=.698$ ).

In our patients, locally advanced rectal cancer T4 tumours were not associated with higher rate of local recurrence in multivariate analysis ( $p=.379$ ). This may be due small sample of patients and small fraction of patients with T4 tumours (12 patients).

This result also was seen in the study of Wasmuth et al. [18] who enrolled 151 patients (8 patients had T4 tumors) with ( $p=.765$ ) in multivariate analysis confirmed that T stage had no value for recurrence.

Unlike the study of Sun et al. [19] 181 patients (the majority of them (108 patients) had T4 tumor), there was a strong link between T4

tumors and local recurrence with ( $p=.001$ ) in multivariate analysis.

We found that positive LNs did not predict local recurrence in multivariate analysis ( $p=.473$ ). Our result was similar to Wasmuth et al. [18] study with one third of 157 patients included had positive nodal involvement ( $n=50$ ) with ( $p=.075$ ) in multivariate analysis for pathological N2 (pN2). This was also seen in Matsuda et al. [20] study and almost half patients with negative nodal involvement (27 of 45 patients) like our study, nodal involvement didn't affect local recurrence rate with ( $p=.567$ ) in multivariate analysis.

But, unlike to our study, Sun et al. [19] study and their 181 patients (94 patients with positive LN (52%)) showed that nodal involvement had significant value on recurrence in multivariate analysis with ( $p=.009$ ). However, in Sun et al. [19] study, positive LNs status was associated with other risk factors of local recurrence like PNI and Lymphovascular invasion (LVI) ( $p=.001$ ).

Poorly differentiated tumor did not show higher rate of local recurrence when compared to well to moderate differentiated tumors in a multivariate analysis ( $p=.083$ ). This was also seen in Zare-Bandamiri et al. [11] study who enrolled 561 patients (66.3% GI, 27.6% GII and 6.1% GIII) in multivariate analysis ( $p=.133$ ).

But our result was against the study by Huang et al. [21] in which poorly differentiated tumors were associated with higher rate of local recurrence after neoadjuvant chemoradiation. In this study, poorly differentiated tumors were associated with higher pathological nodal stage ( $p= .001$ ) and lower response to neoadjuvant CCRT.

In our patients, CRM status wasn't significant for local recurrence in multivariate analysis ( $p=.092$ ).

However, in Agger et al. [22] study, CRM status was a predictive factor for both local recurrence and distant metastasis. Margin  $\leq 1$  mm was a predictive factor for local recurrence ( $p=.017$ ), while there is no difference between margin (1.1-1.9mm) and  $\geq 2$ mm ( $p=.149$ ).

Lymphovascular invasion was not significant for local recurrence in multivariate analysis ( $p=.819$ ). This was also seen in the Wasmuth et al. [18] study in which lymphatic invasion and vascular invasion had no prognostic value on local recurrence with ( $p=.908$ ) and ( $p=.247$ ), respectively.



Unlike Sun et al. [19] study that enrolled 181 patients that showed significant value of LVI on local recurrence rate in multivariate analysis ( $p=.023$ ).

In our study, tumor location in the rectum (upper, middle and lower third) did not have any significant risk for recurrence with ( $p=.636$ ) in Multivariate Cox regression analysis. This result was similar to Hol et al. [23] study that included 159 patients (70% of them located in upper-middle rectum) showed that local recurrence was not higher in low rectal tumors ( $p=.837$ ).

But our result was against the result of the study by Yun et al. [24], in which low rectal tumors had a higher local recurrence ( $p=.001$ ), especially in patients who didn't receive preoperative chemoradiation.

The present study had several limitations. First, this was a retrospective study performed on 100 patients only, which restricts the application and generalization of our findings. Second, bias resulting from this small sample size and excluding other patients who fulfilled the inclusion and exclusion criteria due to incomplete filing and irregular follow up.

## 5. CONCLUSIONS

The present study investigated the value of tumor size as a prognostic factor for local recurrence in patients with rectal adenocarcinoma. Tumor size has a prognostic value in rectal adenocarcinoma. Tumor size  $>5\text{cm}$  is associated with higher rate of local recurrence and worse DFS.

## CONSENT AND ETHICAL APPROVAL

The study was declared for Ethical and Research approval by Tanta University. Signed consent was obtained from all enrolled cases.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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