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Original Research

Correlation between Radiologic Tumor Regression Grading (ycMRI) and Pathological Tumor Regression Grading (ypTRG) in Rectal Cancer

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Aim: To study the correlation between clinical tumor regression grading by MRI (post RT) and the pathological tumor regression grading post neoadjuvant treatment in patients with rectal cancer.

Materials and Methodology: Patients with histopathologically confirmed adenocarcinoma, locally advanced stages non metastatic were included. Exclusion criteria were patients with poor performance status, recurrence and patients with distant metastasis. Patient planned for radiation therapy with 3D conformal radiotherapy technique. Dose prescribed was 50.4Gy in 28 fractions along with Inj. 5FU and Leucovorin every 28 days. MRI was taken 6 weeks after radiation therapy. Tumor regression grading done using TRG score (MRI). Pathologic tumor response assessed by modified Ryan scheme for tumor regression. Correlation between MRI and pathological grading was done using Pearson correlation test.

Results: Among 38 patients, 30 (89%) patients were males and 8 (11%) patients were females. Stage T3 (60.52%) was seen in 23 patients and T4 in 12 (31.57%) patients. Most common stage was IIIB in 23 (60.5%) patients followed by IIIC in 10 (26.3%) patients. 7 patients did not complete the entire course of radiation therapy and 6 patients defaulted for further clinical response assessment. Out of 25 patients, 19 (76%) patients underwent surgery. 6 patients were not willing for surgery due to fear of permanent colostomy. Among the 19 patients who underwent surgery, near complete response and partial response, were seen in 6 (31.6%) patients and 7 (36.9%) patients respectively and no response was seen in 6 (31.6%) patients. Clinical TRG (MRI) correlated well with pathological TRG (r = 0.97, p - 0.000).

Conclusion: Clinical tumor regression grading by MRI correlated well with pathological tumor regression grading in our study. TRG has to be studied more in relevant to patient specific care.

Introduction

Cancer is one of the major non-communicable diseases posing a threat to world health mainly to emerging countries like India. As per GLOBOCAN 2018, colorectal cancers were fourth most common cancer among males and fifth most common among females in India [1]. Magnetic resonance imaging is the most accurate modality in staging rectal cancer [2]. Pretreatment evaluation includes colonoscopy, CEA (carcinoembryonic antigen) and MRI scan. Neoadjuvant chemo-irradiation followed by surgery and adjuvant chemotherapy is the management for locally

advanced rectal cancers.

Treatment is not without morbidities. Surgery may be overtreatment for those who achieved complete response. MRI is helpful in staging, planning treatment and in assessing treatment response. Histological assessment of resected specimen provides the gold standard for assessment of effect of neoadjuvant chemo-irradiation and the degree of pathological response.

Here we attempted to study the correlation between clinical tumor regression grading by MRI (post RT) and the pathological tumor regression grading post neoadjuvant treatment in patients with rectal cancer.

Materials and Methods

Inclusion criteria

Histopathologically confirmed adenocarcinoma, locally advanced stages (Evidence of perirectal fat (cT3- 4) or lymph node involvement (cN+) by either computed tomography or MRI), good performance status (ECOG 0-2), non metastatic. Exclusion criteria were patients with poor performance status, recurrence and patients with distant metastasis. Patients who previously received chemotherapy/ radiotherapy to pelvis were also excluded. Patients with carcinoma rectum presented in RT OPD between April 2021 to August 2022 recruited based on inclusion and exclusion criteria. Complete blood count, liver function test, kidney function test, carcinoembryonic antigen levels (CEA), CT chest and ECHO to assess the cardiac status were done. Colonoscopy was done to evaluate the extent of tumor and rule out synchronous primaries. MRI Abdomen and pelvis was done to assess primary disease and nodal extent. Institutional ethical clearance was obtained.

Patient planned for radiation therapy with 3D conformal radiotherapy technique. Dose prescribed was 50.4Gy in 28 fractions along with Inj.5FU and Leucovorin every 28 days. MRI was taken 6 weeks after radiation therapy. Tumor regression grading done using TRG score as given in Table 1.

Tumor Regression Grade (TRG)	Radiological Response	Features
TRG 1	Complete radiologic response	No evidence of treated tumor
TRG 2	Good response	Dense fibrosis (>75%) no obvious residual tumor,signifying minimal residual disease or no tumor
TRG 3	Moderate response	>50% fibrosis or mucin and visible intermediate signal intensity
TRG 4	Slight response	Little areas of fibrosis or mucin, but mostly tumor
TRG 5	No response	Intermediate signal intensity; same appearance as that of the original tumor

Table 1. Tumor Regression Grading.

Surgery was done and Pathologic tumor response assessed by modified Ryan scheme for tumor regression as given in Table 2.

Description	Tumor regression score
No viable cancer cells (complete response)	0
Single cells or rare small groups of cancer cells (near-complete response)	1
Residual cancer with evident tumor regression, but more than single cells or rare small groups of cancercells (partial response)	2
Extensive residual cancer with no evident tumor regression (poor or no response)	3

Table 2. Modified Ryan Scheme for Tumor Regression Score.

Statistical Analysis

Baseline data like demographics, disease characteristics, comorbidities of the patient are recorded in data entry sheet. Data was analyzed using SPSS 20.0 software. Frequencies and percentages were calculated for discrete variables like age, stage etc. Correlation between clinical and pathological tumor regression grading was studied using Pearson correlation test.

Results

Thirty eight patients were eligible for our study in the given period. Among 38 patients, 30 (89%) patients were males and 8 (11%) patients were females. Median age was 58 years. Most common site was lower rectum involved in 12 patients (31.57%). Stage T3 (60.52%) was seen in 23 patients and T4 in 12 (31.57%) patients. Most common stage was IIIB in 23 (60.52%) patients followed by IIIC in 10 (26.31%) patients.

CRM was positive in 21 (55.26%) patients, threatened in 4 (10.52%) patients and negative in 13 (34.21%) patients. Mesorectal fascia was involved in 21 (55.26%) patients and not involved in 17 (44.73%) patients. 8 (21%) patients underwent diversion colostomy before starting radiotherapy. 7 patients did not complete the entire course of radiation therapy.

Among 31 patients who completed radiation therapy, 6 patients defaulted for further clinical response assessment. Out of 25 patients, 19 (76%) patients underwent surgery, 6 patients were not willing for surgery due to fear of permanent colostomy. Clinical tumour regression score was calculated for 25 patients.

Among MRI (post RT) done 25 patients, Complete clinical response - TRG 1 was seen in 1(4%) patient and he refused for surgery. Good response - TRG 2 seen in 7 (28%) patients. Moderate response - TRG 3 seen in 8 (32%) patients. Slight response - TRG 4 seen in 5 (20%) patients. No response - TRG 5 was seen in 4 (16%) patients.

Among those 4 no response patients, 1 (4%) patient underwent pelvic exenteration. One patient died due to extensive metastases. Two patients started on palliative chemotherapy.

Majority of the patients' i.e., 15 (79%) of them underwent surgery within 8 weeks after completing RT and 4 patients underwent surgery after 8 weeks of completion of RT. Abdominoperineal resection was done in 12 patients (63%), Low anterior resection was done in 5 patients (26 %), pelvic exenteration was done in 1 patient (5%), and proctocolectomy done in 1 patient (5%).

Among 19 patients who underwent surgery, near complete response and partial response, were seen in 6 (31.57%) patients and 7 (36.84%) patients respectively and no response was seen in 6 (31.57%) patients. 1 patient died within 2 weeks of surgery due to postoperative complication and all other patients were given adjuvant chemotherapy (Table 3).

Characteristics:	n (%)
Gender	
Male	17 (79)
Female	2 (21)
Age Group	
30-50 years	6 (32)
>50 years	13 (68)

HPE	
Well differentiated	9 (47.36)
Moderately differentiated	7 (36.84)
Poorly differentiated	2 (15.78)
Stage Grouping	
IIA	1 (5.26)
IIIA	-
IIIB	15 (78.94)
IIIC	3 (15.78)
Site of Tumour	
Upper 1/3RD	2 (10.52)
Middle 1/3RD	3 (15.78)
Lower 1/3RD	5 (26.31)
Upper & Middle 1/3RD	2 (5.26)
Middle & Lower 1/3RD	7 (36.84)
Entire Rectum 1/3RD	1 (5.26)
Pre RT CRM	
Positive (</=1mm)	10 (52.63)
Threatened (1-2mm)	2 (10.52)
Negative (>2mm)	7 (36.84)
Pre RT MRF	
Involved	10 (52.63)
Not Involved	9 (47.36)
Interval Completion of CRT & Surgery	
<8 Weeks	15 (78.94)
>8 Weeks	4 (21.05)
Type of Surgery	
APR	12 (63.15)
LAR	5 (26.31)
others	2 (10.52)
c TRG	
1	-
2	6 (31.57)
3	7 (36.84)
4	5 (26.31)
5	1 (5.26)
p TRG	
0	-
1	6 (31.57)
2	7 (36.84)
3	6 (31.57)

Table 3. Characteristics of Patients who Underwent Surgery.

We analyzed the correlation between MRI grading by TRG and pathological tumor regression grading (p TRG). A strong correlation was found between clinical (MRI) TRG with pathological TRG (r = 0.97), which was found to be statistically significant (p value – 0.000), shown in Table 4.

	Correlations		
		C TRG	P TRG
C TRG	Pearson Correlation	1	.971**
	Sig. (2-tailed)		0
	N	19	19

Table 4. Showing Correlation between cMRI –TRG and pTRG.

Discussion

Organ preservation is evolving concept in management of rectal cancer. Clinical complete response is a crude indicator for organ preservation. There is no agreement on to identify complete response after chemoirradiation [2]. Assessment of post radiotherapy primary by imaging and clinical examination alone may be difficult due to edema, inflammation and fibrosis [3]. Histological assessment is the gold standard for assessment of effect of neoadjuvant chemoirradiation and the degree of pathological response [4].

Fokas et al showed that pTRG (pathological tumor regression grading) is independent predictor of metastasis free and disease free survival [5]. Pathologic response with tumor regression grading after neoadjuvant chemotherapy predicts prognosis and of therapeutic value [6]. Most studies suggested delay of 6 to 8 weeks from the end of chemo-irradiation to the assessment of response is optimal to allow identification of any response. PETCT also showed to predict response post treatment in rectal cancer [7].

MRI is helpful in staging, planning treatment and in assessing treatment response. MRI-TRG (Tumor regression grading) can predict good and poor responders to neoadjuvant chemoirradiation. MRI-TRG 1-3 and MRI-TRG 4-5 are classified as good and poor response respectively [2, 4]. Disadvantage with MRI regression grading is it has interobserver variations. Automatic quantification of fibrosis with MRI is found to be reliable method to identify complete response [2]. Favourable and unfavourable histology can be predicted by both post treatment staging and MRI-TRG [8]. MRI-TRG has been shown that it can be used to predict survival outcomes with good and poor responders [9].

Benzoni et al demonstrated a correlation between c CR and pCR [10]. Similarly in our study also, clinical TRG correlated well with pathological TRG with correlation factor (r = 0.97). Monique Maas et al showed patients with pCR may indicate prognostically favourable biological tumour profile [11].

Rectal cancer can have local recurrences upto 10 years. Pucciarelli et al studied the impact of trans anal excision on local recurrence based on evaluation of pTRG. 3 year cumulative OS, DFS and local DFS were 91.5%, 91% and 96.9% [12].

Most studies suggested delay of 6 to 8 weeks from the end of chemo-irradiation to the assessment of response is optimal to allow identification of any response. Some stated that restaging should be done 8 to 10 weeks after neoadjuvant chemoirradiation will result in higher rate of pathological complete response rate (pCR). Options for increasing pCR rates are several which include lengthening the interval between chemoradiation and surgery, continuous venous infusion of concurrent chemotherapy, additional neoadjuvant chemotherapy, increased radiation doses and boosts and more potent radio sensitisers.

Limitations

Most patients who were fit for surgery, didn’t undergo surgery within the expected period due to covid crisis and also due to fear of permanent colostomy. TRG scoring does not consider nodal response.

In conclusion, clinical tumor regression grading by MRI correlated well with pathological tumour regression grading in our study. More sample size and long term follow up is needed to assess

those patients with good pathological tumour regression. Multi institutional study is required for further validation of our study. TRG has to be studied more in relevant to patient specific care.

Acknowledgments

Statement of Transparency and Principals:

• Author declares no conflict of interest

• Study was approved by Research Ethic Committee of author affiliated Institute.

• Study's data is available upon a reasonable request.

• All authors have contributed to implementation of this research.

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