

Predictors of Tumor Response and Downstaging in Patients Treated with Preoperative Chemoradiation for Rectal Cancer

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Introduction

Preoperative chemoradiation has been shown to be superior to postoperative chemoradiation for stage II and III rectal cancer, in terms of local control, sphincter preservation and toxicity.

The factors that predict tumor response with preoperative chemoradiation for rectal cancer have not been well-characterized.

The goal of this study was to identify factors that predict for pathologic complete response (CR) and tumor downstaging in patients treated with preoperative chemoradiation for rectal cancer.

Methods

- Retrospective analysis on 562 patients with rectal adenocarcinoma and no evidence of metastasis, who were treated with preoperative chemoradiation and mesorectal excision at M.D. Anderson, between November 1989 and July 2004.

- Chi-square tests and logistic regression analysis were performed to identify univariate and multivariate predictors of pathologic CR and T stage downstaging.

- The following potential predictors were evaluated: age, sex, race, clinical T stage, clinical N stage, presence of mucinous features, grade, distance from the anal verge, circumferential extent of tumor, tumor size, anal canal involvement, pretreatment CEA level, radiotherapy dose and type of chemotherapy.

Table 1

Patient, Tumor and Treatment Characteristics	
Median Age (Range)	57.9 years (20.7-87.8 years)
Sex	
Male	354 (63%)
Female	208 (37%)
Clinical T Stage	
T2	31 (6%)
T3	474 (84%)
T4	49 (9%)
Unknown	8 (1%)
Clinical N Stage	
N0	248 (44%)
N1-2	305 (54%)
Unknown	9 (2%)
Median Tumor Size (Range)	5 cm (1-15 cm)
Median Dist from AV (Range)	5 cm (0-12 cm)
Median Circ Extent (Range)	60% (10-100%)
Grade	
Well Differentiated	32 (6%)
Moderately Differentiated	413 (73%)
Poorly Differentiated	33 (6%)
Unknown	84 (15%)
Pathology	
Adenocarcinoma	547 (97%)
Mucinous adenoca	15 (3%)
Median Pretreat CEA (Range)	2.5 ng/mL (0-185 ng/mL)
Median RT Dose (Range)	45 Gy (19.8-58.6 Gy)
Concurrent Chemotherapy	
5-FU	430 (77%)
Capecitabine	114 (20%)
UFT	9 (2%)
Other	9 (2%)

Results

108 (19%) patients had a pathologic CR, 114 (20%) had only microscopic residual disease at surgery, and 340 (61%) had gross residual disease at surgery.

Downstaging of the T stage occurred in 316 (57%) patients. Pathologic T stage was T0 in 20%, T1 in 6%, T2 in 28%, T3 in 39%, and T4 in 5%.

Univariate analysis showed that tumor circumferential extent > 60% and pretreatment CEA level > 2.5 ng/ml were significantly associated with a lower pathologic CR rate.

Univariate analysis showed that tumor circumferential extent > 60%, pretreatment CEA level > 2.5 ng/ml and distance from the anal verge > 5 cm were significantly associated with a lower T downstaging rate.

Multivariate logistic regression analysis showed that greater circumferential extent of tumor independently predicted for a lower pathologic CR rate.

Multivariate logistic regression analysis also showed that greater circumferential extent of tumor and higher distance from the anal verge independently predicted for a lower T downstaging rate.

Table 2

Significant Predictors of Path CR		
	OR	P
Univariate Analysis		
Circumferential extent > 60%	0.53	0.016
CEA > 2.5 ng/ml	0.40	0.010
Multivariate Analysis		
Circumferential extent > 60%	0.31	0.010

Table 3

Significant Predictors of T Downstaging		
	OR	P
Univariate Analysis		
Circumferential extent > 60%	0.51	0.001
CEA > 2.5 ng/ml	0.48	0.006
Distance from AV > 5 cm	0.70	0.035
Multivariate Analysis		
Circumferential extent > 60%	0.49	0.020
Distance from AV > 5 cm	0.46	0.010

Table 4

Rates of Pathologic Response		
	Path CR	Downstaging
Circ extent ≤ 60%	23%	65%
Circ extent > 60%	13%	49%
Dist from AV ≤ 5 cm		61%
Dist from AV > 5 cm		52%

Conclusion

This represents the largest study on predictive factors for pathologic response after preoperative chemoradiation for rectal cancer.

Circumferential extent of tumor was a significant independent clinical predictor of pathologic CR and tumor downstaging on multivariate analysis. Distance from the anal verge independently predicted for tumor downstaging on multivariate analysis. Pretreatment CEA level predicted for pathologic CR and tumor downstaging on univariate analysis.

These factors could be used to help predict outcomes for patients, to develop risk-adapted treatment strategies, and to target patients in trials on newer therapies.