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Original research

Impact of acellular mucin pools on survival in patients with complete pathological response to neoadjuvant treatment in rectal cancer

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HIGHLIGHTS

- The prognostic role of acellular mucin pools in rectal cancer remains to be defined.
- Current recommendation is to consider this as treatment response.
- Current study shows minimal impact of acellular mucin pools on survival in rectal cancer.
- Acellular mucin probably is just a marker of treatment response.

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ABSTRACT

Background: Rarely, patients with pathological complete response (PCR) after neoadjuvant chemoradiotherapy demonstrate acellular mucin pools. The prognostic significance of this finding is controversial. The objective of this study was to determine impact of acellular mucin pools on disease free and overall survival in patients with complete pathological response to neoadjuvant chemoradiotherapy in rectal cancer. **Methods**: One hundred and seventy two patients received neoadjuvant chemoradiotherapy for rectal cancer and underwent surgery. Patients were divided into two groups based on presence of acellular mucin pools. Locoregional failures, distant failures and deaths were compared. Expected 5 year disease free and overall survival was calculated. **Results**: Median follow-up was 36(4–94) months. Complete pathological response was identified in 35(20.3%) patients. Of these, 12(34.2%) had acellular mucin pools in resected specimen. Majority of mucin negative tumors were moderately differentiated (78% vs 25%) ($P = 0.005$). Median overall survival for mucin positive and mucin negative tumors was 4(1.3–5.7) and 3.3(0.1–6.3) years respectively. Expected 5 year disease free and overall survival for mucin positive and mucin negative tumors was 73% and 89% ($P = 0.1$) and 75% and 87% ($P = 0.4$). **Conclusion**: Acellular mucin pools in rectal cancer following a PCR to neoadjuvant treatment do not impact survival.

1. Introduction

Preoperative chemoradiotherapy has emerged as the standard of care in locally advanced rectal cancer [1]. It improves resectability, sphincter preservation and negative margin rates in rectal cancer [1–3]. Complete pathological response (PCR) to preoperative chemoradiotherapy varies between 10 and 20% [4]. A PCR has been linked to improved outcomes. What is not well defined is the prognostic impact of acellular mucin pools in resected rectal specimen after complete pathological response to preoperative chemoradiotherapy. Joint consensus statement by American College of Pathologists recommends not considering acellular mucin pools as residual tumor but the evidence for this recommendation is lacking [5]. Very few studies have specifically dealt with this topic and their results are conflicting compounded by small sample size. Without standardization of criteria of pathological response, results of future prognostic studies and trials would be difficult to interpret. At present, it is not clear whether presence of acellular mucin pools in resected rectal cancer after preop chemoradiotherapy have

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Table 1
Patient characteristics.

		Number ($N = 12$)	Percent %	Number ($N = 23$)	Percent %	P value
Gender	Male	8	67	12	52	0.4
	Female	4	33	11	48	
Family history	Yes	0	0	1	4	0.4
	No	12	100	22	96	
Clinical tumor size	I	1	8	2	8	0.8
	II	8	67	17	74	
	III	3	25	4	18	
Clinical nodal stage	N0	3	25	2	9	0.2
	N1	1	8	6	26	
	N2	8	67	15	65	
Distance from anal verge (centimeter)	5 cm	7	59	16	69	0.8
	6–10 cm	4	33	6	27	
	>10 cm	1	8	1	4	
Surgical procedure	Low anterior resection	6	50	9	39	0.8
	Ultra low anterior resection	1	8	3	13	
	Abdominoperineal resection	5	42	10	44	
	Others	0	0	1	4	
Grade	Well	4	33	1	4	0.005
	Moderate	3	25	18	79	
	Poor	2	17	2	9	
	Mucinous	3	25	1	4	
	Others	0	0	1	4	

an impact on disease free and overall survival in patients after surgery.

The objective of this study was to determine impact of presence of acellular mucin pools in resected specimen of rectal cancer on disease free and overall survival after complete pathological response to neoadjuvant chemoradiotherapy.

2. Methods

During a seven year period from 2005 to 2011, a total of 182 patients underwent resection for underlying rectal cancer. All patients had non metastatic rectal cancer. Patients were discussed in multi-disciplinary meeting and a treatment plan was devised. Thirty four patients did not receive preoperative chemoradiotherapy and were excluded from the study. Eighty nine patients received induction chemotherapy followed by concurrent chemoradiotherapy before surgery while rest had various combinations of preoperative chemo and radiotherapy. Capecitabine based preoperative chemotherapy was used in 114 while 5-Flourouracil based regimen was used in 34 patients. Complete pathological response was defined according to AJCC guidelines as absence of tumor cells in resected rectal specimen or draining lymph nodes. Out of 148 patients, 35 had complete pathological response (pCR) to neoadjuvant treatment. These patients were included in the study and were divided into two groups based on presence of acellular mucin pools in resected rectal specimen. Patient demographics, clinical stage at presentation, histopathological characteristics of tumor and distance from anal verge were compared. Number of locoregional and distant failures and deaths observed during the follow-up period was compared.

Chi square test was used for categorical variables while t test was used for interval variables. Disease free survival was calculated by subtracting date of local, regional or distant recurrence from date of surgery. Overall survival was calculated by subtracting date of death/last follow-up from date of surgery. Expected 5 year survival was calculated using Kaplan Meier curves and significance was determined using Log rank test. A P value <0.05 was considered significant. SPSS version 20 was used for statistical analysis. The hospital ethics committee granted exemption from formal review of this study.

3. Results

3.1. Patient characteristics

Median follow-up was 36(4–94) months. Complete pathological response was observed in 35(21%) patients. Out of these, 12 patients had acellular mucin pools on histopathological examination of resected specimen. No difference was observed between 2 groups with respect to preoperative tumor and nodal stage. Choice of surgical procedure and distance from anal verge was not significantly different between the two groups. A significant difference was observed with respect to grade of tumors and moderately differentiated tumors were seen more frequently in patients with absence of mucin pools (78% vs 25%) ($P = 0.005$). Out of 4 patients with mucinous tumors on pre-treatment biopsy, 3(75%) had acellular mucin pools in resected specimen as shown in Table 1.

3.2. Relapse and mortality

Table 2 represents relapse and mortality. No locoregional relapse was observed in patients with absent acellular mucin pools. One patient with mucin pools had a locoregional relapse. This patient was diagnosed with mucinous adenocarcinoma on endoscopic biopsy before initiation of treatment. Similarly no significant difference was observed between 2 groups with respect to distant relapse and deaths.

3.3. Survival

Median overall survival for mucin positive and mucin negative tumors was 4(1.3–5.7) and 3.3(0.1–6.3) years respectively.

Table 2
Failures (locoregional and distant) and deaths in patients with and without acellular mucin pools after pathological complete response to neoadjuvant chemo radiation.

	Mucin positive ($N = 12$)	Percent %	Mucin negative ($N = 23$)	Percent %	P value
Locoregional	1	8	0	–	0.3
Distant	2	16	1	4	0.2
Deaths	3	25	3	13	0.5