

## RESEARCH ARTICLE

# Prevalence of Local Recurrence of Colorectal Cancer at the Iranian Cancer Institute

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### Abstract

**Background:** Although a great deal of progress has been made in the management of colorectal cancer in terms of neoadjuvant modalities, surgical techniques and adjuvant therapies, the recurrence of tumors remains an enigmatic complication in patients. A better understanding of colorectal cancer and of factors that lead to recurrence of disease can provide helpful information for designing more effective screening and surveillance methods. **Aim:** To investigate the factors that may lead to local recurrence of colorectal cancers. **Materials and Methods:** The current retrospective case study evaluated 617 patients admitted to the Iranian Cancer Institute (the largest referral cancer center in the country) from 1995 to 2009 with confirmed colorectal cancer. Patients with distant metastasis, or with pathology other than adenocarcinoma and no follow-up, were excluded (175 patients). The remainder (442) included 294 (66.5%) with rectal cancer and 148 (33.5%) with colon cancer. The median duration of follow-up was 26 months. **Results:** The total rate of recurrence was 17.4%, comprising 19.6% and 16.3% recurrence rates in colon and rectal cancer, respectively. **Conclusions:** Recurrence of colorectal cancer was significantly correlated to tumor grade ( $p < 0.008$ ).

**Keywords:** Colorectal cancer - recurrence - grade - stage - prevalence - Iran

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### Introduction

Colorectal cancer remains an enormous financial burden on the health care system. Although many new and advanced techniques have been introduced for the management and surveillance of this disease, local recurrence and distant metastasis are still considered major complications. In Iran during the past few decades, there has been both an increase in the prevalence of colorectal cancer and a decrease in the age of onset (Vakili et al., 1976; Fazeli et al., 2007).

It has been shown that the prognosis and survival rate of colon cancer are different from rectal cancer (Wiig et al., 2007; Center et al., 2009; Wang et al., 2010). A thorough knowledge of colorectal cancer would be helpful in establishing better screening and management programs that would improve the quality of life of patients.

Here, the rate of recurrence in patients with confirmed colon cancer is compared with that of patients suffering from rectal cancer who were referred to the Cancer Institute during a 15-year period. Demographic characteristics are also evaluated in order to identify factors that may be involved in recurrence susceptibility.

### Materials and Methods

The medical files of 617 patients treated for colorectal

cancer at the Cancer Institute from March 1995 to March 2009 were evaluated. Ninety-seven patients (15.7%) were excluded from the study as follows: patients with distant metastasis (confirmed with preoperative CT scan and sonography or by intraoperative finding), In addition, 12 (1.9%) patients whose pathology study showed Positive margin from the first surgery, patients with tumors other than adenocarcinoma, 10 (1.6%) (Carcinoid, neuroendocrine and gastrointestinal stromal tumors) and patients with lack of follow up, 56 (9.1%) were also excluded from the study.

A total number of 442 patients were chosen for the study, including 294 (66.5%) with rectal cancer and 148 (33.5%) with colon cancer. Demographic characteristics, tumor location based on endoscopic report, pathology, disease stage and modality of treatment were collected from the files. All patients were operated on by the expert attending. Patients with T3-4 or positive node in pathology reports were treated with 5-fluorouracil based chemotherapy and for rectal cancer, with the same stage, radiotherapy concurrently added to the mentioned regimen total doses of 45-50 gray in 25-28 divided fractions was used, concurrently with 5FU as a radiosensitizer. Since 2005 according to institute protocol, all rectal cancers with T3-4 or positive node in pre-operation staging workup (detected by CT scan and endosonography) have been treated with neoadjuvant chemoradiation followed by

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adjuvant 5FU based chemotherapy

Median follow-up time was 26 months. The routine follow-up in our institute consists of a physical exam every 3 or 4 months in addition to running a CEA (carcinoembryonic antigen) test for the first two years after the initial surgery, then every 6 months for the next 3 years. Colonoscopy, abdominopelvic sonography or CT scan and chest radiography are performed at the end of the first year following surgery. The presence of a tumor based on clinical, pathological, laboratory or radiological findings, and confirmed by a biopsy after the initial curative surgery, is considered as tumor recurrence. All data were analyzed by SPSS 11.5 and we used the Chi-square test for assessing the relationship of type of cancer and categorical variables and independent samples t test for assessing this relationship with numerical variables. P value  $\leq 0.05$  was considered statistically significant. Our study was approved by the Research Ethics Committee of Tehran University of Medical Sciences.

## Results

Tumor recurrence was detected in 77 patients (17.4%) CI 95% (13.9-21.0%) out of a total of 442 patients. Twenty-nine out of 148 patients with colon cancer (19.6%) CI 95% (12.1-20.6%) and 48 (16.3%) CI 95% (13.2-26.0%) out of 294 patients in the rectal cancer group (Table 1). Patients and tumor characteristics with recurrence are shown in Table 1.

The median follow-up time was 26 months (14-63). There was no difference in terms of sex and age distribution among patients with recurrence of colon and rectal cancer. Overall recurrence rate was 17.4% including 19.6% of patients with colon cancer and 16.3% of rectal cancer patients. In addition, there were no significant differences in both groups of patients in terms of stage of disease, musin staining and blood groups. The grade

of tumor was significantly correlated with recurrence in colon and rectal cancer ( $p < 0.008$ ).

## Discussion

Recurrence of cancer is tragic for both patients and the medical team. Recurrence in rectal carcinoma is scarcely tolerable for patients because there is a higher risk of permanent stoma that may lead to pelvic exenteration and increased morbidity in patients because of deep pelvic abscess, delay in perineum healing and leakage (Wiig et al., 2007; Ferenschild et al., 2009).

Andreoni et al (2007) showed that recurrence in rectal cancer is significantly higher than with colon cancer (14% versus 6.1%;  $p < 0.001$ ). In addition, a study by Li M et al (2008) demonstrated that the recurrence of rectal cancer is 1.5 times higher than colon cancer.

In the current study we did not find any significant difference in rate of recurrence between rectal and colon cancer patients. Our findings are compatible with another study by Kreamer et al (2001) which showed that the site of the original tumor does not affect recurrence rate of colorectal cancers.

Beside, similar to Nadoshan et al (2013) study, sex had no effect on recurrence.

Inconsistent findings regarding the rate of recurrence in colorectal carcinoma might be explained by different preoperative staging, and by variations in neoadjuvant regimens plus inconsistent treatment modalities throughout the world, as discussed in Knut et al (2010).

We did not find any correlation between recurrence and disease stage. This may be related to incomplete surgical staging (inadequate harvested lymph nodes), incorrect assessment of lymph nodes and different staging systems being used during the study period (1995-2009). It should be mentioned that proper radical surgical resection (total mesorectal excision) and neoadjuvant therapies in recent years mainly influence the staging of colorectal cancer (Staib et al., 2002).

Neoadjuvant therapy plays an important role in reduction of local recurrence of rectal cancer (Doll et al., 2009; Hansen et al., 2009). However, in the Iranian population colorectal cancers have shown a shift to the left side of the colon (Omranipour et al., 2012) and we also reported higher number of rectal cancers in the current study. There has been no significant increase in colon cancer recurrence compared to rectal cancer.

Although histological grading plays a significant role in disease prognosis (Greene et al., 2002), it is not part of the TNM classification (Compton et al., 2002). Our study also demonstrates a high correlation between tumor grading and recurrence ( $p < 0.008$ ).

We did not find any effect on tumor musin production and recurrence that is similar to findings in studies performed by other groups (Enriquez et al., 1998; Farhat et al., 2008). Beside Farhat et al (2008) showed that colorectal mucinous adenocarcinoma is present with high grade tumors compared to non-mucinous ones. Moreover, studies on the prognosis of mucinous tumors showed no effect of age, tumor staging or grading on the prognosis. In contrast to the aforementioned study, Messerini et al

**Table 1. Tumor Characteristics of Patients with Recurrence**

	Total (%)	Recurrence (%)		p value
		Colon	Rectum	
No Of Patients With Recurrence	77 (17.4)	29 (19.6)	48 (16.3)	0.43
Sex				0.09
	M	42 (19.1)	18 (25.4)	24 (16.1)
	F	35 (16.1)	11 (14.3)	24 (17.1)
Age Mean [Std.Dev]	53.58 [15.64]	54.86 [14.99]	52.9 [15.94]	0.54
Stage				0.46
	I-Ii	35 (14.6)	16 (18.2)	19 (12.6)
	Iii	40 (22.0)	13 (23.2)	27 (21.4)
Grade				0.008
	Low	44 (14.1)	19 (15.6)	25 (13.2)
	Med-Hi	33 (26.4)	10 (38.5)	23 (23.2)
Musin+(Positive) Abo(Percent)	21(22.8)	5 (20.0)	16 (23.9)	0.95
	A	24 (18.9)	7 (17.5)	17 (19.5)
	B	21 (22.6)	8 (24.2)	13 (18.8)
	Ab	6 (20.7)	3 (23.1)	3 (21.7)
	O	26 (12.5)	11 (16.7)	15 (10.4)
Rh (Percent)				0.62
	Positive	69 (17.51)	25 (19.23)	44 (16.66)
	Negative	8 (16.66)	4 (22.22)	4 (13.33)

(1995); Cusack et al (1996) demonstrated that mucinous carcinoma has a poorer prognosis, higher recurrence and shorter survival time. Finally, another study by Adsay et al (2005). showed that various types of mucinous carcinoma affect disease prognosis differently.

In previous studies, no association was made between blood group and the risk of colorectal cancer Khalili et al (2011). A study by Halvorsen (1986) also supports this finding although it demonstrates that patients with positive rhesus types had more metastasis to lymph nodes. Our study did not find any association between blood group or rhesus types with recurrence of colorectal cancer.

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