CHANGES IN PROFILE AND COLORECTAL CANCER STAGE OVER 15 YEARS IN PUERTO RICO

Introduction: The stage of a malignant tumor defines how advanced the malignant process is at the time of diagnosis. In many clinical scenarios it is an indirect measurement of the efficacy of screening interventions used for early detection. We have evaluated changes in the tumor-node-metastasis (TNM) stage of colorectal cancer across a 15-year period.

Methods: This was a retrospective study in which all patients who underwent colorectal cancer surgery at the HIMA San Pablo Medical Center in 1988–1990 (period 1) and 2002–2004 (period 2) had their pathological report examined. The TNM stage for all patients was examined by using standard criteria.

Results: A total of 285 patients were evaluated: 108 in period 1 and 177 in period 2. The number of patients >71 years of age who underwent colon surgery increased (33% vs 46%). An increase in patients with stage one colon cancer was observed in period 2 (30% vs 10%) with a corresponding decrease in stage 2 and 3 (59% vs 83%).

Conclusion: The pathologic and demographic profile of patients with colorectal cancer has changed over 15 years. Patients with colon cancer are younger and have an earlier stage of disease with a decrease in lymph node involvement. Patients with rectal cancer were older and more likely to be men. (*Ethn Dis.* 2008;18[Suppl 2]:S2-128–S2-131)

Key Words: Colon Cancer, Rectal Cancer, Screening, TNM Staging

From the Retrovirus Research Center, Internal Medicine Department, Universidad Central del Caribe, University Hospital Ramón Ruiz Arnau (MCA, IL, DH, DMF, RQ, RFHM); Department of Pathology, San Pablo Hospital (JS), Bayamón, Puerto Rico.

Address correspondence and reprint requests to: Robert Hunter Mellado, MD, MSc, FACP; Retrovirus Research Center; Universidad Central del Caribe; PO Box 60327; Bayamón, PR 00960-6032; 787-787-8710; 787-787-8733; robert.hunter@ uccaribe.edu Marinely Cruz-Amy, MD; Juan Serrano, MD; Ismael Labrador, MD; David Hernandez, MD; Diana M. Fernandez, MS, EdD; Rafael Quintana, MPH; Robert F. Hunter-Mellado, MD

INTRODUCTION

Establishing the stage of a malignant tumor can define the prognosis of individual patients and aid in the choice of appropriate therapeutic modalities. The value of any staging system is to establish a survival advantage of individual patients at the time of diagnosis by instituting appropriate therapy. In this study, we evaluated changes in the age, sex, and cancer stage patients with colorectal cancer at two different time intervals.

The staging of colorectal tumors has undergone significant changes between the two time periods we aim to study. A number of tumor-related characteristics are used to define the individual stage of malignant tumors. These include the site of the primary lesion, size, and extent of growth, histological type, and histological grade. When variables are combined, the prognostic ability is significantly enhanced.

Since the description of the first practical staging system by Dukes,¹ staging systems have evolved. The availability of different staging systems to classify tumor presentation across time makes a direct comparison of a cohort of patients difficult because of differences in the definition of the variables used in each staging system^{2,3}. Thus proper comparison of any cohort of colorectal cancer patients across time makes it necessary to recompute the stage of tumor with a uniform system.^{4,12}

During the last 15 years, the introduction of aggressive screening interventions—fecal occult blood testing and direct colonic visualization—have played an important role in the earlier detection of colorectal cancer. In addition, the introduction of colorectal surgery as a certified subspecialty may have changed the nature and extent of surgical specimens available for staging.^{6,13–15} Both of these factors may modify the presenting stage of patients with colorectal cancer.^{5,16} We believe that if screening has become more effective, colorectal tumors would have been down-staged after 15 years.⁷

In this study, we examined the stage of the malignant process in a cohort of patients who underwent colorectal surgery in the San Pablo Medical Center in 1988–1990 and 2002–2004. We evaluate differences in the tumor-nodemetastasis (TNM) stage presentation of colorectal cancer, along with the age and sex of patients at the time of the surgical intervention.

MATERIALS AND METHODS

Study Population

We evaluated all patients who underwent colorectal cancer surgery during 1988-1990 (period 1) and 2002-2004 (period 2) in the San Pablo Medical Center Hospital in Bayamón, Puerto Rico. A total of 286 pathology records that met the inclusion criteria for the study were included for analysis. Patients were excluded if a surgical excision was not performed. Surgical resection was defined as a procedure in which the primary tumor and draining lymph nodes were removed and reported by the pathologist. Each worksheet was assigned a specific number for purposes of confidentiality and for internal control. The worksheet included the pathological record number in order to allow future access to the report in the future if necessary. All patients

were stratified and restaged using the TNM staging system.⁹ This normalization of the stage allowed us to compare the stages of patients across the time period examined. The TNM staging system compartmentalizes carcinomas according to the depth of invasion of the primary tumor, the absence or presence of regional lymph node metastases, and the absence or presence of distant metastases.⁹

We have stratified and compared our study cohorts by using the following variables: age at presentation, sex, type of surgeon (general vs colorectal surgeon), and stage at presentation. In addition we analyzed colon and rectal cancer as separate entities, considering that in many cases preoperative radiotherapy is used to downstage rectal cancer patients.¹⁰ We also evaluated the number of regional lymph nodes examined in the surgical specimen. These have been stratified the following way: group 0: no nodules removed, group I: 1-3 nodules removed, group II: 4-9 nodules removed, and group III >10 nodules removed. This study was evaluated and approved by our institutional review board.

Statistical Analysis

For purposes of analysis we separated colon cancer from rectal cancer. A descriptive analysis was performed by using SPSS 14.0 (SPSS, Inc., Chicago, Ill). In order to determine the association between the different variables, the χ^2 test of independence was used.

RESULTS

A total of 286 patients met the inclusion criteria, 109 in period 1 and 177 in period 2. The median age was 68 years in the first period and 66 years in the second period. We stratified and compared the age of patients at presentation: \leq 54 years of age, 55–70 years , and \geq 71 years . In Tables 1 and 2 we present a comparison of age, sex, and

	Age <i>n</i> (%)	Sex	Surgeon
Period 1		Period 1	Period 1
≤54 years	10 (14.7%)	Males	General
55–70 years	27 (39.7%)	32 (47.1%)	57 (83.8%)
≥71 years	31 (45.6%)	Females	Colorectal
		36 (52.9%)	6 (8.8%)
Period 2		Period 2	Period 2
≤54 years	18 (13.5%)	Males	General
55–70 years	71 (53.4%)	62 (46.6%)	45 (33.8%)
≥71 years	44 (33.1%)	Females	Colorectal
		71 (53.4%)	87 (65.4%)
	P = .101	P = .953	P = .011

Table 1.Colon cancer

type of surgeon performing the procedure in both periods.

The sex distribution for colon cancer was similar in both periods, but for rectal cancer more men were seen in the second period (60% vs 77.3%) (P=.087).

We evaluated the training of the surgeon on record for all patients in both periods (Table 1 and 2). As anticipated, more procedures were performed by colorectal surgeons in the second period for colon cancer (65.4% vs 8.8%) (P=.011) and for rectal cancer (75% vs 22%). In the second period, colorectal surgeons were more likely to operate on patients with a lower stage of disease than were general surgeons (Table 3).

We compared and analyzed the presenting pathological stage of colon and rectal cancer between the two periods of time. More patients presented with earlier-stage disease in the second period (Table 3), although no differences were seen in patients with stage 4 cancer. As shown in Table 3, similar trends were observed for rectal cancer, with a decrease in patients with stages 2 and 3; nevertheless, the use of preoperative radiotherapy was prevalent in our community during the second period, which may have downstaged patients with rectal tumors.

We analyzed the presence or absence of positive lymph nodes as a function of the period of time, the age of the patient, and sex (Table 4). In the first period, 52.9% of patients had at least one positive lymph node as compared to 38.5% in the second period (P=.076). This finding was not observed in patients with rectal tumors. Younger patients (<70 years) were observed to have a higher percent of positive lymph nodes in both colon and rectal tumors (44% and 36% vs 39.1% and 28.6%) (P=.436 and .620). In colon cancer,

Table 2. Rectal cancer

	Age <i>n</i> (%)	Sex	Surgeon
Period 1		Period 1	Period 1
≤54 years	8 (19.5%)	Males	General
55–70 years	15 (36.6%)	24 (60.0%)	29 (70.7%)
≥71 years	18 (43.9%)	Females	Colorectal
,		16 (40.0%)	9 (22%)
Period 2		Period 2	Period 2
≤54 years	5 (11.4%)	Males	General
55–70 years	20 (45.5%)	34 (77.3%)	11 (25%)
≥71 years	19 (43.2%)	Females	Colorectal
,		10 (22.7%)	33 (75%)
	P = .514	P = .087	P = .315

/1 0	^o				
	TNM staging	Colorectal surgeon	General surgeon	P value	
Colon: Period 1				.303‡	
tage0	1(1.5%)	0	1(1.8%)		
tage1	7(10.4%)	2(33.3%)	4(7.1%)		
tage2	33(49.3%)	2(33.3%)	27(48.2%)		
tage3	22(32.8%)	1(16.7%)	21(37.5%)		
tage4	4(6%)	1(16.7%)	3(5.4%)		
olon: Period 2				.011+	
age0	2(1.5%)	2(2.3%)	0		
tage1	40(30.1%)	35(40.2%)	5(11.1%)		
tage2	47(35.3%)	23(26.4%)	24(53.3%)		
tage3	32(24.1%)	18(20.7%)	13(28.9%)		
tage4	12(9%)	9(10.3%)	3(6.7%)		
-	P=.024*				
ectal: Period 1				.908‡	
age0	0	0	0		
age1	4(9.8%)	1(11.1%)	3(10.3%)		
age2	24(58.5%)	4(44.4%)	18(62.1%)		
age3	12(29.3%)	4(44.4%)	7(24.1%)		
age4	1(2.4%)	0	1(3.4%)		
ectal: Period 2				.315‡	
tage0	1(2.3%)	1(3%)	0		
tage1	11(25%)	10(30.3%)	1(9.1%)		
tage2	21(47.7%)	15(45.5%)	6(54.5%)		
tage3	8(18.2%)	6(18.2%)	2(18.2%)		
age4	3(6.8%)	1(3%)	2(18.2%)		
-	P=.187†				

Table 3.	Type of surgeon vs	colon and rectal	I cancer tumor-node-metastasis (TNM) stage
Table J.	Type of surgeon vs	colon and recta	i cancer tumor-noue-metastasis (114/4) stage

 \ast Differences between Periods and stages of colon cancer.

† Differences between periods and stages of rectal cancer.

‡ Differences between general vs. colo-rectal surgeon per period.

males were more often found with positive lymph nodes than females (49.4% vs 36.7%) (P=.86). This later finding was not observed in rectal tumors. Although not statistically significant, the data suggest trends in the demographic profile of the patients who underwent the surgical resection and should be further evaluated with a greater number of patients.

CONCLUSIONS

More colon cancer surgeries were performed at our institution in 2000– 2004 than in 1988–1990, perhaps because of an increase in colorectal cancer screening. The fact that more patients presented with lower-stage colon cancer in the second period supports this hypothesis. Nevertheless,

Table 4.	Analysis of	positive lympł	nodes com	pared to perio	od, age, and sex
i uoic ii	/ und	positive tymp	i nouco com	purcu to pern	su, age, and sex

	Colon cancer	P value	Rectal cancer	P value
Period 1	52.9%	.076	34.6%	.982
Period 2	38.5%		34.9%	
Age				
≤70 years old	44%	.436	36%	.620
\geq 71 years old	39.1%		28.6%	
Sex				.867
Males	49.4%	.086	35.4%	
Females	36.7%		33.3%	

the number of rectal tumors was similar in both periods. This finding is perplexing, since more effective screening practices, which include fecal occult blood testing and flexible sigmoidoscopy, should lead to an increase in the detection of rectal tumors compared with colon tumors.^{8,18} An additional point is that several reports suggests that the location of primary colonic tumors are shifting towards the right side of the colon. Our data is consistent with this if rectal tumors are excluded from the analysis.¹⁷

We observed a tendency toward an increase in the number of younger patients undergoing surgery for both colon and rectal cancer. This tendency was more pronounced in patients aged 55–70 years for colon cancer, but it did not reach significance. No significant differences in the gender distribution between the two periods were observed for colon cancer or rectal cancer. This finding may indicate that screening interventions are available and implemented in both sexes, arguing against the existence of a healthcare disparity on the basis of sex.¹⁹ Nevertheless, in absolute numbers, more men than women had rectal cancer diagnosed in period 2. A plausible explanation may be related to an increase in digital rectal examinations related to the availability of the prostatic antigen blood test(PSA) during the second period. The presence of marginally abnormal PSA test was available and frequently used during the second period of our study. Abnormal PSA tests could have led to an increased in the frequency of DRE, which would have led to increased detection of rectal cancer. Additional studies should determine whether the availability of the prostate-specific antigen test as a routine part of the male exam is contributing to an increase in digital rectal examination

With the introduction of colorectal surgery as a subspecialty in our hospital, we expected to see an increase in the number of earlier-stage patients, as these would be referred to colorectal surgeons for intervention. In patients with colon cancer, we found an increase of 56.6% in the referral to colorectal surgeons in the second period as hypothesized. This was accompanied by a decrease in the number of patients being managed by general surgeons. A similar finding was observed among patients with rectal cancer. Both findings were accompanied by an expected increase in the numbers of patients with earlier-stage tumors, particularly those in which a colorectal surgeon were involved. We believe that one of the reasons general surgeons are faced with patients having a more advanced stage of disease may be related to an increase exposure of these surgeons to situations in which more emergent interventions are required. Emergent situations include events such as colonic obstructions or patients presenting with more painful or symptomatic disease. The general finding of our study, nevertheless, is that the presenting tumor stage for both colon and rectal cancer in the second period represented an earlier tumor-node-metastasis stage as compared to the first period of time.

In this study we also analyzed the presence and number of positive lymph nodes removed during the cancer surgery. A decrease in the percent of positive lymph nodes was seen during the second period for colon cancer patients but no difference in patients with rectal cancer. We also observed a higher percentage of positive lymph nodes in patients <70 years of age for both colon and rectal cancer. Finally, males were more frequently seen with positive lymph nodes than females, which may mean that males are being screened for cancer at a more advanced stage of disease.

ACKNOWLEDGMENTS

This research was supported by RCMI/NIH Grant Number G12RR03035 and CDC-ASD-AIDS Surveillance Section Grant Number U62/CCU206209. The authors would like to thank Ms. Magaly Torres, and Research staff of HIV Data Core.

References

- 1. Dukes CE. The classification of cancer of the rectum. *J Pathol Bacteriol*. 1932;35:323–32.
- Fleming ID, Cooper JS, Henson DE, Hutter RVP, Kennedy BJ, Murphy GP, et al. *American Joint Committee on Cancer. Cancer Staging Manual.* 5th edition. Philadelphia: Lippincott-Raven; 1997.
- Gastrointestinal Tumor Study Group. Adyuvant therapy of the colon cancer: results of a prospectively randomized trial. *N Engl J Med.* 1984;310:737–43.
- Nanthanson SD, Schultz L, Tiller, et al. Carcinoma of the Colon and rectum: A comparison of staging classifications. *Am. Surg.* 1986;52:539–543.
- Comptom CC, Greene FL. The staging of colorectal cancer: 2004 and beyond. *Ca Cancer J Clin.* 2004;54:295–308.

- Chapman AE, Levitt MD, Hewett P, Woods R, Sheiner H, Maddern GJ. Laparoscopicassisted resection of colorectal malignancies: a systematic review. *Ann Surg.* 2001;234: 590–606.
- Walsh JME, Terdiman JP. Colorectal cancer screening: clinical applications. *JAMA*. 2003; 289:1297–1302.
- Maule WF, Bruzzi JF, Brennan DD, Fenlon HM, Sood A, Sood R, Ransohoff DF, Sandler RS. Screening for colorectal cancer. *N Engl J Med.* 2002;346:1672–1674.
- American Joint Committee on Cancer. Colon and rectum. In: *Manual for Staging of Cancer*, Bearhs D, Hutter HR, eds. Philadelphia: JD Lippincott; 1988:75–80.
- Vokes E, Weichselbaum R. Concomitant chemoradiotherapy: rationale and clinical experience in patients with solid tumors. *J Clin Oncol.* 1990;8:911–920.
- Gastrointestinal Tumor Study Group. Survival after postoperative combination treatment of rectal cancer. *New Engl J Med.* 1986;315: 1294–1295.
- Lindblom A. MD. Improved tumor staging in colorectal cancer. *New Engl J Med.* 1998;339: 264–265.
- Winawer SJ, Andrews MNA, Flehinger B, Sherlock P, Schottenfeld D, Miller DG. Progress report on controlled trial of fecal occult blood testing for the detection of colorectal neoplasia. *Cancer.* 1980;45:2959–2964.
- Winawer SJ, Flehinger BJ, Schottenfeld D, Miller DG. Screening for colorectal cancer with fecal occult blood testing and sigmoidoscopy. J Natl Cancer Inst. 1993;85:1311–1318.
- Selby JV, Friedman GD, Quesenberry CP Jr, Weiss NS. A case-control study of screening sigmoidoscopy and mortality from colorectal cancer. N Engl J Med. 1992;326:653–657.
- Allison JE, Feldman R, Tekawa IS. Hemoccult screening in detecting colorectal neoplasm: sensitivity, specificity, and predictive value: long-term follow-up in a large group practice setting. *Ann Intern Med.* 1990;112:328–333.
- Chattar-Cora D, Onime GD, Valentine IS, Rivera-Cora L. The anatomic distribution of colorectal cancer in a New York City Puerto Rican group. *Bol Asoc Med P R.* 1998; 90(7–12):126–129.
- Strum WB. Impact of a family history of colorectal cancer on age at diagnosis, anatomic location, and clinical characteristics of colorectal cancer. *Int J Gastrointest Cancer*. 2005; 35(2):121–126.
- Theuer CP, Taylor TH, Brewster WR, et al. The topography of colorectal cancer varies by race/ethnicity and affects the utility of flexible sigmoidoscopy. *Am Surg.* 2001;67(12):1157–1161.