EUROPEAN JOURNAL OF CLINICAL & MEDICAL ONCOLOGY ORIGINAL ARTICLE

Epidemiology of Colorectal Cancer in Turkey: A Cross-sectional Disease Registry Study (A Turkish Oncology Group Trial)

NF Aykan[1], Ş Yalcin[2], NS Turhal[3], M Ozdogan[4], G Demir[5], M Ozkan[6], A Yaren[7], C Camci[8], H Akbulut[9], M Artac[10], N Meydan[11], K Uygun[12], A Isikdogan[13], D Unsal[14], O Ozyilkan[15], A Arican[16], E Seyrek[17], SB Tekin[18], O Manavoglu[19], A Ozet[20], T Elkiran[21], and R Disci[22]

Affiliations: [1]Department of Medical Oncology, Institute of Oncology, Istanbul University, Istanbul, Turkey; [2]Department of Medical Oncology, Institute of Oncology, Hacettepe University, Ankara, Turkey; [3]Department of Medical Oncology, Marmara University School of Medicine, Istanbul, Turkey; [4]Department of Medical Oncology, Akdeniz University School of Medicine, Antalya, Turkey; [5]Department of Medical Oncology, School of Medicine, Istanbul Bilim University, Istanbul, Turkey; [6]Department of Medical Oncology, Erciyes University School of Medicine, Kayseri, Turkey; [7]Department of Medical Oncology, Pamukkale University School of Medicine, Denizli, Turkey; [8]Department of Medical Oncology, Gaziantep University School of Medicine, Gaziantep, Turkey; [9]Department of Medical Oncology, Ankara University School of Medicine, Ankara, Turkey; [10]Department of Medical Oncology, Selcuk University School of Medicine, Konya, Turkey; [11]Department of Medical Oncology, Adnan Menderes University School of Medicine, Aydin, Turkey; [12]Department of Medical Oncology, Kocaeli University School of Medicine, Kocaeli, Turkey; [13]Department of Medical Oncology, Dicle University School of Medicine, Diyarbakir, Turkey; [14]Department of Radiation Oncology, Gazi University School of Medicine, Ankara, Turkey; [15]Department of Medical Oncology, Baskent University School of Medicine, Adana, Turkey; [16]Department of Medical Oncology, Inönü University School of Medicine, Malatya, Turkey; [17]Department of Medical Oncology, Mersin University School of Medicine, Icel, Turkey; [18]Department of Medical Oncology, Atatürk University School of Medicine, Erzurum, Turkey; [19]Department of Medical Oncology, Uludag University School of Medicine, Bursa, Turkey; [20]Department of Medical Oncology, Gulhane Military Medical School, Ankara, Turkey; [21]Department of Medical Oncology, Firat University School of Medicine, Elazig, Turkey and [22]Department of Cancer Epidemiology and Biostatistics, Istanbul University, Institute of Oncology, Istanbul, Turkey

ABSTRACT

PURPOSE

This study aimed to determine the profile of recently diagnosed colorectal cancer patients in Turkey.

PATIENTS AND METHODS

In this multicenter, prospective, and cross-sectional registry study, data for 968 patients with colorectal cancer from 21 centers in 7 geographic regions of Turkey were analyzed.

RESULTS

Diagnosis was colon cancer (CC) in 662 (68.4%) and rectum cancer (RC) in 306 (31.6%) patients. In total, 60.9% of patients were male; mean age was 58.9 ± 12.6 years. Among patients, 15.0% were drinking alcohol, 17.5% were smoking, 1.5% had familial history of polyposis, 15.0% had diabetes mellitus, and 1.0% had inflammatory bowel disease. Fruit and vegetable consumption was low (< 3 times/week) in 35.5% and red meat consumption was high (≥ 3 times/week) in 47.4% of the patients. Median duration between first symptoms and diagnosis was 3.0 and 4.0 months for patients with CC and RC, respectively. Mean body mass index was > 25 in all group of patients. Distal rectum (61.3%) and sigmoid colon (36.8%) were the most common locations of cancer. In total, 85.6% of patients were operated; 25.8% had emergency surgery. Low anterior resection rate was 64.2% in RC. In majority (89.8%) of the patients with RC who received preoperative treatment, conventional chemo-radiotherapy regimen was given. pathologic Tumor Nodes Metastasis (pTNM) staging at diagnosis showed that stages III and IV patients were in majority (35.9% and 29.7%, respectively).

CONCLUSIONS

CC is more frequent than RC in Turkey. Colorectal cancer patients are diagnosed at later stages. Most of the cases were operated. Interregional differences for risk factors are worthwhile for evaluation in future trials.

Keywords: colorectal cancer, epidemiology, risk factors, Turkey

Correspondence: Nuri Faruk Aykan, Institute of Oncology, Istanbul University, 34390 Capa Istanbul, Turkey. Tel: +90 212 414 24 34; Fax: +90 212 661 59 53; e-mail: nfaruk@mac.com

INTRODUCTION

Colorectal cancer is among the most common type of cancers worldwide. According to the Global Cancer database (GLOBOCAN) 2008, which is published by the International Agency for Research on Cancer to estimate the worldwide incidence and mortality of 27 cancers from 182 countries, colorectal cancer (1.23 million, 9.7% of the total) is the third most commonly diagnosed cancers worldwide following lung (1.61 million, 12.7%) and breast (1.38 million, 10.9%)

cancers.[1] Although incidence and mortality of colorectal cancers have been decreasing since 1985, the worldwide incidence is still up to 20.4 for men and 14.7 for women with a mortality rate of 9.7 and 7.0 per 100 000 persons per year. In the less developed regions, the incidence of colorectal cancers for men and women is 12.1 and 9.4 per 100 000 persons per year. However, in the developed regions, this incidence for men and women increases to 37.7 and 24.3 per 100 000 persons per year.[1,2] Colorectal cancer is the second commonest cause of death from any cancer in men in the European Union following the lung cancer.[3]

According to Turkish Ministry of Health 2004–2006 Cancer Statistics, the age-standardized incidence rate of colorectal cancer in Turkey is 17.0 in men and 11.7 in women per 100 000 persons.[4,5] The estimated number of new colorectal cancer patients in both sexes is 7218 (4102 male, 3116 female) in Turkey, according to the GLOBOCAN 2008 data.[6]

Incidence of colorectal cancer changes with populations and time.[7–10] Populations living in one community whose lifestyles also differ from those of others in the same community also experience different levels of colorectal cancer.[3] Ethnic and racial differences in colorectal cancer suggest that genetic and environmental factors including cultural, social, and lifestyle practices play a major part in the etiology of the disease.[3] Therefore, population-specific epidemiological data are important to define etiology of colorectal cancer and to develop national policies for prevention, diagnosis, and treatment of this highly common type of cancer.

In Turkey, an extensive epidemiological study on the profile of patients with colorectal cancer and diagnostic and treatment approaches is not available. By this cross-sectional prospective registry study, it was aimed to determine the socio-demographic, clinical, and biological profile of colorectal cancer patients in Turkey, and to evaluate differences between colon cancer (CC) and rectum cancer (RC) in terms of these characteristics.

PATIENTS AND METHODS

Study Design and Population

This was a prospective national, multicenter, and cross-sectional disease registry study. There was no investigational treatment and/or any intervention to the treatment methods applicable to this study. As inclusion criteria, between 13 October 2008 and 14 October 2009 (defined 1-year period), patients over 18 years of age with the diagnosis of histologically confirmed colorectal cancer were eligible in the study from medical oncology departments of 21 centers in 7 geographic regions of Turkey. Each patient signed an informed consent form before enrollment to the study. They were not exclusion criteria.

The study was conducted in accordance with Good Epidemiological Practice, Good Clinical Practice, and local requirements. The study was approved by Local Ethics Committee of the coordinating center and Ministry of Health of Turkish Republic.

Study Data

Patients were evaluated in one study visit, no follow-up visit was performed. Following data were collected during study visit: socio-demographics, familial cancer history, medical history, time between the initial symptoms and diagnosis, diagnostic tests, tumor markers, localization of tumor, surgery (time, type, blood transfusion), pathology (macroscopy, histological tumor staging, grade, lymph nodes, lymphovascular and neural invasion), and pTNM staging. Preoperative standard work-up procedures (endoscopy and biopsy, CT and/MRI, laboratory tests) were mandatory for all centers. Diagnostic methods used to evaluate metastasis were also questioned.

Statistical Methods

Study data were presented with descriptive statistics (eg, mean, median, standard deviation, range, number, percentage). Data of CC and RC patients were analyzed separately. Quantitative and qualitative data were compared with *t*-test and chi-square test, respectively. Statistical level of significance was accepted as $P < .05$.

RESULTS

Patients

Of the 1057 screened patients, 968 (60.9% male; mean age, 58.9 ± 12.6 years) were eligible complying with inclusion criteria and included in the study (**Figure 1**). Median number of analyzed patients per center was 31 (2–176). Only four centers registered <10 patients. A number of analyzed patients of centers and their represented geographical regions are shown in **Table 1**. Diagnosis was CC in 662 (68.4%) patients and RC in 306 (31.6%) patients.

Socio-demographics

Male patients were predominant with a rate of 60.7% among CC patients and 61.4% with RC patients (**Table 2**). Patients with RC were younger than those with CC ($P = 0.011$; **Figure 2**). CC was the most common in the Marmara region with 198 patients (29.9%) and RC was most common in the Central Anatolia with 81 cases (26.5%). CC had significantly high percentage than RC in the Mediterranean region (17.7%

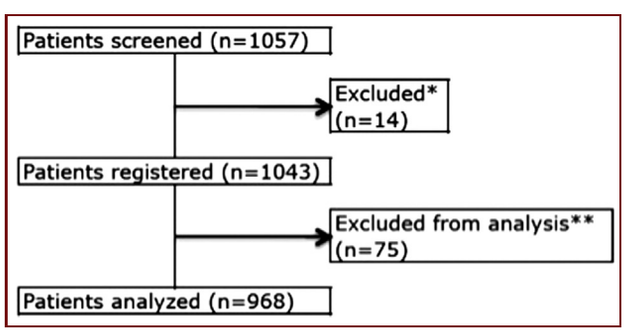

Figure 1. Consort diagram. (*): Patients who declined to participate, (**): Patients who did not meet the inclusion criteria.

Table 1. Number of Analyzed Patients of Centers and their Represented Geographical Regions

Geographical Regions	Cities	Number of Representing Centers	Number of Analyzed Patients
Marmara	Istanbul, Bursa, Kocaeli	5	278
Black Sea		(2)[a]	62
Aegean	Aydin, Denizli	2	97
Central Anatolia	Ankara, Konya, Kayseri	6	265
Eastern Anatolia	Erzurum, Elazig, Malatya	3	40
Mediterranean	Antalya, Icel, Adana	3	154
Southeastern Anatolia	Gaziantep, Diyarbakir	2	72

[a]Patients from Black Sea region are registered in the centers of Istanbul and Ankara.

Table 2. Socio-demographical characteristics of study patients

	CC	RC
	n = 662	n = 306
Gender[a]		
Female	260 (39.3%)	118 (38.6%)
Male	402 (60.7%)	188 (61.4%)
Mean age (years)[b]	59.63 ± 12.47	57.43 ± 12.75
Age distribution (years)		
18–30	16 (2.4%)	6 (1.9%)
31–40	37 (5.6%)	28 (9.1%)
41–50	92 (13.9%)	53 (17.3%)
51–60	188 (28.4%)	92 (30.1%)
61–70	197 (29.8%)	82 (26.8%)
71–80	113 (17.1%)	36 (11.8%)
>81	19 (2.9%)	9 (2.9%)
Geographical regions[c]		
Marmara	198 (29.9%)	80 (26.1%)
Black Sea	31 (4.7%)	31 (10.1%)
Aegean	65 (9.8%)	32 (10.5%)
Central Anatolia	184 (27.8%)	81 (26.5%)
Eastern Anatolia	18 (2.7%)	22 (7.2%)
Mediterranean	117 (17.7%)	37 (12.1%)
Southeastern Anatolia	49 (7.4%)	23 (7.5%)
Living area[a]		
Town	92 (13.9%)	49 (16%)
Village	47 (7.1%)	27 (8.8%)
City	497 (75.1%)	225 (73.5%)
Unknown	26 (3.9%)	5 (1.6%)

[a]Not significant.
[b]$P = 0.011$.
[c]$P < 0.001$.

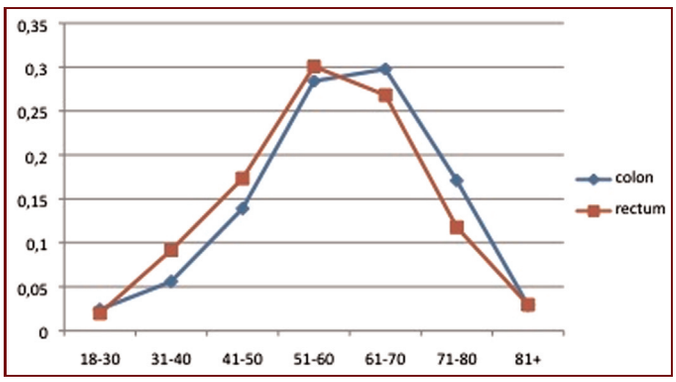

Figure 2. Age distribution of patients with colon and RC.

vs 12.1%) while RC was higher in the Eastern Anatolia (7.2% vs 2.7%) and Black Sea regions (10.1% vs 4.7%; $P < 0.001$).

Medical history, physical evaluation, and risk factors for colorectal cancer

The ECOG performance status of 629 (66.5%) patients was 0. Almost half ($N = 463$, 49.4%) of the patients had not lost weight while 152 (16.2%) lost 10 or more than 10 kg in the last 6 months. In 23% of the patients who had weight loss, the loss was approximately 1–5 kg. Weight loss was similar between CC and RC groups (**Table 3**).

Hemoglobin level was significantly lower in CC than RC (11.9 ± 2.2 vs 12.8 ± 1.8 g/dL; $P < 0.003$; **Table 3**).

Among 968 patients, 145 (15.0%) were regularly drinking alcohol for 25.7 ± 12.5 years, and 169 (17.5%) were currently smoking. Familial history for cancer was slightly higher in RC (34.7% vs 37.9%, respectively), and familial history for colorectal cancer (7.4% vs 5.6%, respectively) was higher in CC patients (**Table 3**).

Among 968 patients, 145 (15.0%) had diabetes mellitus, 96 (9.9%) had dyslipidemia, 283 (29.2%) had hypertension, and 93 (9.6%) had coronary arterial disease. Ten patients (1.0%) had inflammatory bowel disease (**Table 3**).

Fruit and vegetable consumption was high (≥3 times/week) for 64.5% of patients and red meat consumption was low (<3 times/week) for 52.6% of the patients (**Table 4**). Red meat consumption was significantly higher in Marmara, Central Anatolia, and Eastern Anatolia regions than in Aegean and Mediterranean regions (**Table 5**).

Diagnosis of Colorectal Cancer

The median duration between first symptoms and diagnosis was 3.0 months (range 1.0–48.0 months) and 4.0 months (range 1.0–48.0 months) for CC and RC patients, respectively (**Table 6**).

In endoscopic examination, primary tumor location for colon was sigmoid colon (36.8%), cecum (10.1%), ascending colon (9.7%), descending colon (8.1%), and transverse colon (7.1%). Primary location for RC was distal rectum (61.3%), medial rectum (13.5%), and proximal rectum (7.4%).

Table 3. Medical history, physical findings, and risk factors for colorectal cancer

	CC (N = 662)	RC (N = 306)	P value
ECOG performance status			
0	424 (65.9%)	205 (67.7%)	NS
1	167 (26.0%)	82 (27.1%)	
2	40 (6.2%)	14 (4.6%)	
3	10 (1.6%)	2 (0.7%)	
4	2 (0.3%)	–	
Body mass index (mean ± SD, kg/m²)	25.8 ± 4.2	25.7 ± 4.4	NS
Weight loss during last six months (kg)	3.9 ± 5.2	3.4 ± 4.6	NS
Hemoglobin (mean ± SD, g/dL)			
Male	11.9 ± 2.2	12.8 ± 1.8	.001
Female	10.9 ± 1.9	11.5 ± 1.5	.003
Cigarette smoking			
Non-smoker	369 (55.7%)	159 (52.0%)	
Former smoker	187 (28.3%)	84 (27.4%)	
Currently smoking	106 (16.0%)	63 (20.6%)	.098
Alcohol consumption			
Drinking	99 (14.9%)	46 (15.0%)	NS
Not drinking	563 (85.1%)	260 (85.0%)	
Family history for colorectal cancer[a]	49 (7.4%)	17 (5.6%)	NS
Family history for cancer	230 (34.7%)	116 (37.9%)	NS
Familial polyposis	7 (1.1%)	8 (2.6%)	NS
Lynch syndrome	1 (0.2%)	3 (0.9%)	NS
Inflammatory bowel disease			
Ulcerative colitis	5 (0.8%)	2 (0.6%)	NS
Crohn's disease	3 (0.4%)	0	NS
Concomitant diseases			
Hypertension	205 (31.0%)	78 (25.5%)	NS
Diabetes mellitus	104 (15.7%)	41 (13.4%)	NS
Coronary arterial disease	68 (10.3%)	25 (8.2%)	NS
Dyslipidemia	68 (10.3%)	28 (9.1%)	NS
Others	149 (22.5%)	55 (18.0%)	–

[a]In the first-degree relatives, ≤50 years of age. SD: Standard deviation, NS: Not significant.

Preoperative evaluation of tumor markers such as Carcinoembryonic Antigen (CEA) and Carbohydrate Antigen (CA) 19–9 was performed in 476 (49.0%) and 433 (44.7%) patients, respectively. Considering CEA levels <5 ng/mL as normal for smoking and <2.5 ng/mL for nonsmoking patients, preoperative CEA was pathological in 214 (69.3%) CC patients and in 98 (61.6%) RC patients. Considering CA 19–9 levels between 0 and 37 IU/mL as normal, preoperative CA 19–9 was abnormal in 88 (31.6%) CC patients and in 32 (20.6%) RC patients.

Table 4. Red meat and fruit/vegetable consumption in terms of cancer type

	CC N = 662 (%)	RC N = 306 (%)
Red meat consumption		
High (≥3 times/week)	242 (36.6)	121 (39.5)
Low (<3 times/week)	350 (52.9)	159 (52.0)
None	70 (10.6)	26 (8.5)
Fruits and vegetables in diet		
High (≥3 times/week)	411 (62.1)	213 (69.6)
Low (<3 times/week)	184 (27.8)	72 (23.5)
None	67 (10.1)	21 (6.9)

Preoperative endoscopic ultrasonography (EUS) and pelvic magnetic resonance imaging (MRI) were performed in 46 (15.0%) and 76 (24.8%) of RC patients, respectively.

Major diagnostic method used to evaluate metastasis was computerized tomography (CT) scan with 94.8%. Positron Emission Tomography (PET) is used 2.2% for this aim.

Treatment of Colorectal Cancer

Surgery

In total, 829 of 968 (85.6%) patients were operated (**Table 7**). Of these patients, 214 (25.8%) had emergency surgery while 615 (74.2%) had elective surgery. The ratio of the patients who have gone to emergent surgery was higher in CC patients than RC patients (29.7% vs 16.7%, P < .001). Among the 829 patients who were operated, 587 (70.8%) had radical surgery, 156 (18.8%) had explorative surgery (diagnostic laparotomy), and 86 (10.4%) had palliative surgery. The ratio of the patients who had radical surgery was higher in RC group (76.4% vs 68.4%, P = .026).

The most common surgical method was open surgery (93.3%) in CC patients and low anterior resection (64.2%) in RC patients. Metastasectomy was performed in 40 (16.3%) of the metastatic patients.

Table 5. Red meat consumption by geographical regions

	Low (<3 times/week) N = 509 (%)	High (≥3 times/week) N = 363 (%)	P-value
Marmara	127 (25)	125 (34.4)	.002
Black Sea	25 (4.9)	28 (7.7)	NS
Aegean	64 (12.6)	23 (6.3)	.002
Central Anatolia	122 (24)	112 (30.9)	.02
Eastern Anatolia	14 (2.8)	24 (6.6)	.007
Mediterranean	116 (22.8)	23 (6.3)	<.001
Southeastern Anatolia	41 (8.1)	28 (7.7)	NS

NS: Not significant.

Table 6. Symptom to diagnosis duration

	CC	RC
	N = 662 (%)	N = 306 (%)
0–3 months	299 (56.2)	124 (49.4)
4–6 months	119 (22.4)	65 (25.9)
7–12 months	80 (15.0)	44 (17.5)
13–24 months	31 (5.8)	14 (5.6)
≥25 months	3 (0.6)	4 (1.6)
Total	532 (100.0)	251 (100.0)

Chemotherapy and radiotherapy

Preoperatively, 77 (25.8%) RC patients received chemoradiotherapy, 13 (4.2%) had chemotherapy, and 9 (2.9%) had radiotherapy. Rest of RC patients (N = 205, 66.9%) have not received any preoperative treatment. Radiotherapy and bolus 5-fluorouracil were applied to 30 (37.9%), and radiotherapy and 5-fluorouracil continous infusion were applied to 46 (58.2%) patients. Only 3 patients (3.7%) received radiotherapy and oral Fluoropyrimidine (FP) preoperatively. In majority (N = 79, 89.8%) of the patients who received preoperative radiotherapy, conventional regimen for 25 days was administered, while 5 × 5 Swedish regimen was given in only 9 (10.2%) patients.

Pathological Findings

In both CC and RC patients, ulcero-vegetative form was the most frequently (29.2%) seen macroscopic type of the tumor

Table 7. Details of surgical treatment of colorectal cancer

	CC	RC	
	N = 662 (%)	N = 306 (%)	P-value
Operated	583 (88.1)	246 (80.4)	.002
Emergency operation	173 (29.7)	41 (16.7)	<.001
Type of surgery			
Explorative	119 (20.4)	37 (15.0)	
Palliative	65 (11.1)	21 (8.5)	
Radical	399 (68.4)	188 (76.4)	.026
Surgical methods			
Open	544 (93.3)	–	
Laparoscopic	34 (5.8)	–	
Mixed (Hand assistant)	4 (0.7)	–	
Endoscopic resection	1 (0.2)	–	
Low anterior resection	–	158 (64.2)	
Abdomino-perineal resection	–	55 (22.4)	
Local excision	–	11 (4.5)	
Hartmann	–	2 (0.7)	
Other	–	20 (8.2)	
Stent	5 (0.8)	13 (4.2)	<.001
Blood transfusion	131 (22.5)	57 (23.2)	NS

NS: Not significant.

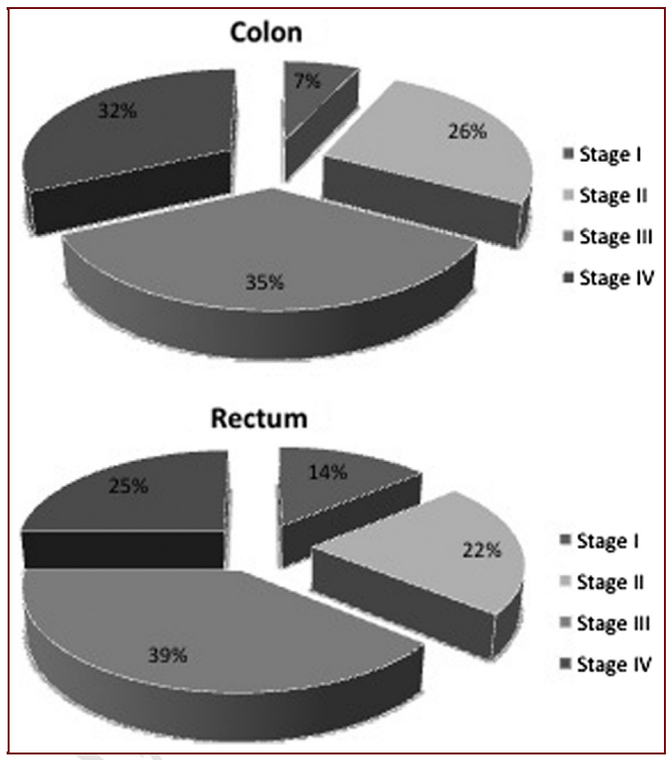

Figure 3. American Joint Committee on Cancer/Tumor Nodes Metastasis (AJCC/TNM) staging for colon and RC patients.

(**Table 8**). Microscopic evaluation showed that among all colorectal cancer patients, 18.3% were well differentiated (G1), 44.8% were moderately differentiated (G2), 13.3% were poorly differentiated (G3). Lympho-vascular and neural invasion were positive in 320 (33.1%) and 213 (22.0%) of all colorectal cancer patients, respectively. In both CC and RC group of patients, subserosa involvement (pT3) was the most frequently (55.4%) seen degree of invasion for the primary tumor. Median number of dissected lymph nodes was 13 (range 0–99) and mean value of maximum size of involved node was 1.91 mm. The percentage of node negative (pN0) and node positive (pN1 and pN2) patients was 30.7% and 43.9%, respectively in all patients.

Disease Staging

For 142 (14.7%) patients who cannot be assessed optimally (due to pTx, pNx and/or Mx) disease could not be staged. **Figure 3** shows AJCC (TNM) pathological staging of total 826 patients (580 CC, 246 RC). Among 826 patients, 297 stage III cancer patients were in majority (35.9%). In CC group, the incidence of distant metastasis (M1) was higher than RC group (31.7% vs 24.7%, P = 0.046). Liver was the most common metastatic site (57.7%).

DISCUSSION

Cancer registry studies provide the main data to develop strategies for improving our understanding of cancer and for development of national policies and guidelines for prevention, diagnosis, and treatment of cancer. In this

Table 8. Pathological findings of colorectal cancer

	CC (N = 662)	RC (N = 306)
Macroscopic types		
Fungiform	49 (7.4%)	58 (18.9%)
Infiltrative	86 (12.9%)	41 (13.4%)
Papillary	2 (0.3%)	4 (1.3%)
Polypoid	93 (14.1%)	30 (9.8%)
Ulcerative	124 (18.7%)	70 (22.9%)
Ulcero-vegetative	192 (29%)	91 (29.7%)
Unknown	116 (17.5%)	12 (3.9%)
Differentiation		
G1	126 (19.0%)	51 (16.7%)
G2	281 (42.4%)	153 (50%)
G3	89 (13.4%)	40 (13.0%)
G4	4 (0.6%)	–
GX	162 (24.5%)	62 (20.3%)
Lymphovascular invasion	229 (34.6%)	91 (29.7%)
Neural invasion	147 (22.2%)	66 (21.6%)
Number of lymph nodes (mean ± SD)		
Resected	16.7 ± 15.6	12.3 ± 10.6
Metastatic	2.4 ± 5.2	2.3 ± 4.4
Immunoreactive	10.2 ± 13.8	7.0 ± 9.2
Maximum size of metastatic lymph node (mm)	1.7 ± 5.9	2.3 ± 7.9
Primary tumor staging		
TX	108 (16.3%)	63 (20.6%)
To	2 (0.3%)	4 (1.3%)
Tis	2 (0.3%)	–
T1	9 (1.3%)	5 (1.6%)
T2	52 (7.9%)	47 (15.3%)
T3	384 (58.0%)	152 (49.7%)
T4	105 (15.9%)	35 (11.4%)
Regional lymph nodes		
NX	159 (24.0%)	87 (28.4%)
No	204 (30.8%)	93 (30.4%)
N1	168 (25.4%)	67 (21.9%)
N2	131 (19.8%)	59 (19.3%)
Distant metastasis		
Mo	416 (62.8%)	201 (65.7%)
M1	184 (27.8%)	61 (19.9%)
Mx	62 (9.4%)	44 (14.4%)
Metastatic sites		
Liver	141 (56.6%)	50 (61.0%)
Abdominal wall (peritoneum + omentum)	41 (16.5%)	4 (4.9%)
Lung (pleura)	24 (9.6%)	14 (17.1%)
Lymph nodes (intra-abdominal)	17 (6.8%)	6 (7.3%)
Others	26 (12.2%)	8 (9.8%)

cross-sectional registry study, we determined the profile of colorectal cancer patients in Turkey.

The GLOBOCAN 2008 database reveals that 12.7 million new cancer cases and 7.6 million cancer deaths occurred in 2008, with 56% of new cancer cases and 63% of the cancer deaths occurring in the less developed regions of the world.[1] Colorectal cancer is among the most common cancers worldwide with high mortality rate. It is estimated that colorectal cancer is the fourth most common cause of death from cancer worldwide.[10] Colorectal cancer is the fourth most common cancer (6.9% of total) in men and second in women (8.1%) in Turkey.[4,5]

In spite of high incidence rate of colorectal cancer in Turkey, there are a few studies in the literature on the epidemiology of colorectal cancers in Turkey, which presented data of colorectal cancer patients from a single center.[11,12] The present report is the first prospective long-term registry study determining the general profile of colorectal cancer patients in Turkey.

Twenty-five centers representing the country geographically were invited to enroll new colorectal cancer patients during one-year period, and 968 patients from medical oncology departments of 21 centers were included in the study. Demographic characteristics of patients were in line with the previous epidemiological data of colorectal cancers. Mean age of patients was 58.9 ± 12.6 years, and 60.9% were male. It is known that more than 90% of colorectal cancer cases occur in people aged 50 or older.[10,13] Yilmazlar *et al.*[11] and Zorluoglu *et al.*[12] who were both from same center (Uludag University, Bursa in Marmara region) also reported in their retrospective data that young patients (<40–45 years old) accounted for only 20% of all colorectal cancer patients in Turkey. This ratio was 8.9% in our serial, and age distribution showed that patients with RC were younger than those with CC.

In our study population, CC was more frequent (68.4%) than RC (31.6%). Indeed, in a 21-year registry of colorectal cancer, Ponz de Leon *et al.*[14] reported a tendency over time toward a progressive increase of colonic tumors and a decrease in rectal neoplasms. Among the geographical regions of Turkey, CC was the most common in the Marmara region with 198 patients (29.9%), and RC was most common in the Central Anatolia with 81 cases (26.5%) in all country. CC had significantly high proportion than RC in the Mediterranean region (17.7% versus 12.1%), while RC was higher in the Eastern Anatolia (7.2% versus 2.7%) and Black Sea regions (10.1% versus 4.7%) ($P < 0.001$) (**Table 1**). But, when we look at the percentage of CC and RC separately in

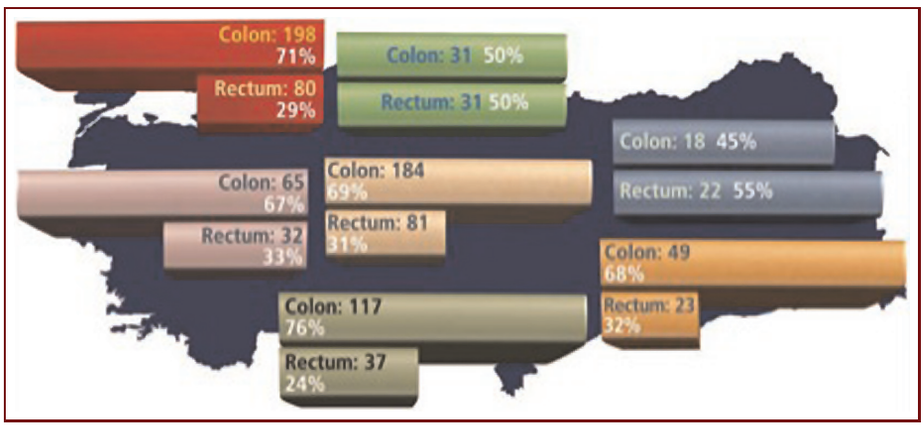

Figure 4. Distribution of colon and RC patients by regions.

each region outside total population, in spite of low number of patients, the ratio of colon and RC was equal in the Black Sea region, CC was higher in the other five regions except Eastern Anatolia where the highest percentage of RC was observed (55% vs 45%) (**Figure 4**). These inter-regional differences of relative percentage between CC and RC cases may be due to lifestyle factors. For example, red meat consumption was significantly high in Marmara, Central and Eastern Anatolia regions. On the other hand, the percentage of smoking patients was slightly higher but not significant in RC group. The role of red meat consumption and smoking should be elucidated in future trials to understand inter-regional differences of risk factors.

In the previous studies, age, obesity, diabetes mellitus, family history, hereditary conditions, inflammatory bowel disease, diet (consumption of red and processed meat, diet low in fruits and vegetable), and lifestyle factors (physical activity, alcohol in-take, and smoking) were positively correlated with the risk of colorectal cancers.[7,13,15–17] It was also reported that long-term ulcerative colitis and Crohn's disease increase the risk of developing colorectal cancer.[18,19] In terms of these risk factors, 15.0% of our study population was regularly drinking alcohol, 17.5% was currently smoking, 1.5% had positive familial history of polyposis, 15.0% had diabetes mellitus, and 1.0% had inflammatory bowel disease. Mean body mass index was greater than the upper limit in our patient population although approximately 4-kg weight loss during last 6 months. Fruit and vegetable consumption was low (<3 times/week) in 35.5% of patients, and red meat consumption was high (≥ 3 times/week) in 47.4% of the patients. Patients with CC and RC had no clinically significant difference in terms of risk factors. Among the RC patients, more patients were currently smoking (20.6%), but this was not statistically significant ($P = 0.098$). Family history did not show any accumulation of inherited colorectal cancer cases in our patients.

As a physical finding, anemia was significantly more frequent in patients with CC in both sex as well ($P < 0.005$). It is known that anemia is a most common sign of right-sided color cancers.[20,21]

We found that the median duration between first symptoms and diagnosis was 3.0 months and 4.0 months for patients with CC and RC, respectively. Yilmazlar *et al.*[11] retrospectively reviewed 46 patients under 40 years old and reported that the mean duration of time from the onset of symptoms to diagnosis was 5.8 months. The shorter time to diagnosis in our study may be due to difference in study designs, sample sizes, and increased awareness for early diagnosis over time. Our findings showed that distal rectum was the most common location for RC and sigmoid colon was the most common location for CC. This finding was similar to studies published with an interval of nearly 10 years by Yilmazlar *et al.*[11] and Zorluoglu *et al.*[12] who reported that colorectal tumor was localized at the sigmoid and the rectum in 74–80% of cases.

Preoperative evaluation of tumor markers such as CEA and CA 19–9 was performed in around 45% of patients, while EUS and MRI were performed in 15.0% and 24.8% of the patients with RC, respectively. This is not sufficient in terms of preoperative work-up for clinical staging and needs improvements.

Quality of surgery and pathology is extremely important in the management of colorectal cancer. Median number of dissected lymph nodes was 13 in all group of patients; this is an acceptable value for the accuracy of pathological staging; it should be minimum 12.[22] The ultimate goals of surgery in the modern management of RC are the improving local control and overall survival, maintaining quality of life and preserving sphincter, genitourinary, and sexual functions.[23] For this purpose, total mesorectal excision (TME) with autonomic nerve preservation via low anterior resection (LAR) is the treatment of choice for appropriate patients with RC.[23–25] TME was applied in 41.3% of RC patients in our serial and LAR ratio was 64.2%. There was no information in pathology reports about TME surgery in 39% of our patients.

In patients with transmural and/or node-positive disease (T3/T4 and/or N+) with no distant metastases, preoperative chemoradiation is widely accepted.[23] Preoperatively, 25.8% of patients with RC received chemoradiotherapy in this trial. There was not cTNM information for this subgroup of patients, and pTNM staging demonstrated 39% stage III

disease; this reflects that postoperative chemoradiotherapy is still an option in some centers.

Patients were diagnosed at a considerably later stage (as 35.9% patients were at stage III, 29.7% patients were at stage IV) and most of the cases (85.6%) were operated. Mainly, 70.8% of patients had radical surgery. Thus, majority of patients were referring to medical oncology clinics after receiving surgical treatment. In the study by Cook *et al.*[26] surgical resection was applied in 66% of stage 4 colorectal cancer patients. In our study, 25.8% of operated patients had emergency surgery while 74.2% had elective surgery. In the study by Zorluoglu *et al.*,[12] 6.6% of 136 patients were operated emergently, and the rest (93.3%) were operated electively.

Among patients who have colorectal cancer, approximately 50% will eventually develop liver metastases.[16] The proportion of colorectal cancer patients with synchronous liver metastases was reported as 14.5%.[27] We found that 33.2% of patients had metastasis and liver was the most common metastatic site (57.7%). Metastasectomy was performed in 40 (16.3%) of the metastatic patients.

This study has some limitations. First and main limitation of the present study is its cross-sectional design. Considering that this is the first large registry study reporting colorectal cancer profile in Turkey, further prospective surveys including patients across the country would provide definite data on the epidemiology of colorectal cancer in Turkey. Secondly, the present data are from medical oncology departments as registration centers in this study. More mature data can be obtained by adding departments of surgery in future trials.

As a conclusion, CC is more frequent than RC in Turkey. Patients with colorectal cancer are diagnosed at considerably later stages and most of the cases are operated. Although, operative, preoperative, and post-operative standard procedures as well as pathological evaluations are satisfactory, but they need improvements. The role of the consumption of red meat, obesity, metabolic syndrome, diabetes mellitus, and smoking as risk factors for colorectal cancers as well as interregional differences should be evaluated in further prospective trials with larger sample size.

Acknowledgements: The authors would like to thank the staff of Monitor Medical Research and Consulting (Istanbul, Turkey) for study operation and Sanofi-Aventis Turkey for funding the statistical analysis.

Disclosure: There are no financial disclosures from any authors.

REFERENCES

1. Ferlay J, Shin HR, Bray F, *et al*. *GLOBOCAN 2008 v1.2, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 10*. Lyon, France: International Agency for Research on Cancer. http://globocan.iarc.fr. 2010. [Accessed 22 August 2011].
2. Ferlay J, Shin HR, Bray F, *et al*. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer*. 2010;127:2893–2917.
3. Boyle P, Longman JS. ABC of colorectal cancer: epidemiology. *BMJ*. 2000;321:805–808.
4. Eser SY. Cancer incidence in Turkey. In: Tuncer M, editor. Cancer Control in Turkey. Ankara: Ministry of Health Publication, 2008:17–44.
5. Eser S, Yakut C, Özdemir R, *et al*. Cancer incidence rates in Turkey in 2006: a detailed registry based estimation. *Asian Pac J Cancer Prev*. 2010;11:1731–1739.
6. Ferlay J, Shin HR, Bray F, *et al*. GLOBOCAN 2008 v2.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 10, Lyon, France; 2010, http://globocan.iarc.fr/factsheet.asp, accessed on 28/11/2012.
7. Yee YK, Tan VP, Chan P, *et al*. Epidemiology of colorectal cancer in Asia. *J Gastroenterol Hepatol*. 2009;24:1810–1816.
8. Malekzadeh R, Bishehsari F, Mahdavinia M, Ansari R. Epidemiology and molecular genetics of colorectal cancer in Iran: a review. *Arch Iran Med*. 2009;12:161–169.
9. Rim SH, Seeff L, Ahmed F, *et al*. Colorectal cancer incidence in the United States, 1999–2004: an updated analysis of data from the National Program of Cancer Registries and the Surveillance, Epidemiology, and End Results Program. *Cancer*. 2009;115:1967–1976.
10. Haggar FA, Boushey RP. Colorectal cancer epidemiology: incidence, mortality, survival, and risk factors. *Clin Colon Rectal Surg*. 2009;22:191–197.
11. Yilmazlar T, Zorluoglu A, Ozguc H, *et al*. Colorectal cancer in young adults. *Tumori*. 1995;81:230–233.
12. Zorluoglu A, Yilmazlar T, Ozguc H, *et al*. Colorectal cancers under 45 years of age. *Hepatogastroenterology*. 2004;51:118–120.
13. Amersi F, Agustin M, Ko CY. Colorectal cancer: epidemiology, risk factors, and health services. *Clin Colon Rectal Surg*. 2005;18:133–1340.
14. Ponz de Leon M, Rossi G, di Gregorio C, *et al*. Epidemiology of colorectal cancer: the 21-year experience of a specialized registry. *Intern Emerg Med*. 2007;2:269–279.
15. Hill LB, O'Connell JB, Ko CY. Colorectal cancer: epidemiology and health services research. *Surg Oncol Clin N Am*. 2006;15:21–37.
16. Benson AB. III. Epidemiology, disease progression, and economic burden of colorectal cancer. *J Manag Care Pharm*. 2007;13(6 Suppl C): S5–S18.
17. Watson AJM, Collins PD. Colon cancer: a civilization disorder. *Dig Dis*. 2011;29:222–228.
18. Triantafillidis JK, Nasioulas G, Kosmidis PA. Colorectal cancer and inflammatory bowel disease: epidemiology, risk factors, mechanisms of carcinogenesis and prevention strategies. *Anticancer Res*. 2009;29:2727–2737.
19. Loftus EV Jr. Epidemiology and risk factors for colorectal dysplasia and cancer in ulcerative colitis. *Gastroenterol Clin North Am*. 2006;35:517–531.
20. Prichard PJ, Tjandra JJ. Colorectal cancer. *Med J Aust*. 1998;169:493–498.
21. Sadahiro S, Suzuki T, Tokunaga N, *et al*. Anemia in patients with colorectal cancer. *J Gastroenterol*. 1998;33:488–494.
22. Compton CC, Greene FL. The staging of colorectal cancer: 2004 and beyond. *CA Cancer J Clin*. 2004;54:295–308.
23. Geibel J, Longo W. Modern management of rectal cancer: a 2006 update. *World J Gastroenterol*. 2006;12:3186–3195.
24. Baxter NN, Garcia-Aguilar J. Organ preservation for rectal cancer. *J Clin Oncol*. 2007;25:1014–1020.
25. Guillem JG, Cohen AM. Current issues in colorectal cancer surgery. *Semin Oncol*. 1999;26:505–513.
26. Cook AD, Single R, McCahill LE. Surgical resection of primary tumors in patients who present with stage IV colorectal cancer: an analysis of surveillance, epidemiology, and end results data, 1988 to 2000. *Ann Surg Oncol*. 2005;12:637–645.
27. Manfredi S, Lepage C, Hatem C, *et al*. Epidemiology and management of liver metastases from colorectal cancer. *Ann Surg*. 2006;244:254–259.