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Do Young Colon Cancer Patients Have Worse Outcomes?

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Abstract. Previous studies on colon cancer have noted rising incidence rates among young individuals and suggest that they may have more aggressive disease and worse 5-year survivals than their older counterparts. Our study uses a nationwide population-based cancer registry to analyze colon cancer presentations and outcomes in a young versus an older population. The records of patients with colon carcinoma were obtained from the Surveillance, Epidemiology, and End Results (SEER) national cancer database (1991–1999). Two cohorts based on age at diagnosis (20–40 years, $n = 1334$ vs. 60–80 years, $n = 46{,}457$) were compared for patient and tumor characteristics, treatment, and 5-year cancer-specific survival. A multivariate Cox regression was performed to identify predictors of survival. The young group had a higher proportion of black and Hispanic patients than did the older group ($p < 0.001$). Young patients had less stage I or II disease, more stage III or IV disease ($p < 0.001$), and worse-grade (poorly differentiated or anaplastic) tumors ($p < 0.001$). The 5-year stage-specific survival was similar for stage I and III disease (p = NS) but was significantly better for young patients with stage II and IV disease ($p < 0.01$). Using a nationally representative cancer registry, we found that young colon cancer patients tend to have later-stage and higher-grade tumors. However, they have equivalent or better 5-year cancer-specific survival compared to older patients. This population-based finding contradicts prior single-institution reports.

Colon cancer is the most common malignancy of the gastrointestinal tract. Along with rectal cancer, it is the third most commonly diagnosed cancer and the second leading cause of cancer-related deaths (for both sexes) in the United States. According to the American Cancer Society, an estimated 107,300 new cases of colon cancer would have been diagnosed in 2002, and 48,100 patients would have died from this disease [1–4].

In general, colon cancer is thought of as a disease of the older population, with more than 90% of patients being diagnosed after age 55 [5]. It also occurs in the young population, however, with approximately 3% of cases being diagnosed in patients between the ages of 20 and 40 [6]. Of particular interest is that the incidence of colon cancer in young patients (20–40 years) has been rising over the past 25 years [7].

Many articles have previously reported poor outcomes for young colon cancer patients relative to the older population. These young patients have been portrayed as having more aggressive disease (i.e., more advanced stage and grade) and a worse 5-year survival. However, these studies tend to be small and reflect single-institution experiences, which may have various biases including smaller sample sizes as well as patient selection or referral patterns.

Because of these potential limitations, we evaluated the status of colon cancer in the young at a national, population-based level. The current study analyzed differences in (1) patient demographics, (2) cancer-related data, and (3) survival between young and older colon cancer patients using a nationwide, population-based data sample.

Materials and Methods

All patients diagnosed with colon cancer in the Surveillance, Epidemiology, and End Results (SEER) national cancer registry from 1991 to 1999 were evaluated. Benign, in situ, rectal, and appendiceal tumors were excluded. Specific histologies were selected by the *International Classification of Diseases for Oncology*, 2nd edition (ICD-9) coding and were chosen to include adenocarcinoma, mucinous, and signet-ring cell histologies. Carcinoids, sarcomas, and lymphomas were excluded.

Data were then organized into two age categories: a young cohort (20–40 years) and an older cohort (60–80 years). These two age groups were chosen to (1) capture those "young" patients well below the screening age of 50, and (2) select an "older" group who should ideally be screened by age 60.

Patient Demographics

Demographic information recorded for each patient included age, gender, race/ethnicity (white, black, Hispanic, Asian, "other"), and marital status (single versus married at diagnosis).

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Cancer-related Data

Cancer-specific data evaluated for each patient included tumor location, stage at presentation, tumor grade, specific histology, receipt of cancer-directed surgery, and radiation treatment. Tumor location was organized into three categories: right colon (cecum, ascending colon, and hepatic flexure), transverse colon (transverse colon only), and left colon (splenic flexure, descending colon, and sigmoid colon).

Tumor stage was evaluated using the American Joint Committee on Cancer (AJCC) staging system (stages I–IV). Tumor grade was classified as: well differentiated, moderately differentiated, poorly differentiated, and undifferentiated or anaplastic. Separate analyses were performed for the specific histologies of mucinous and signet-ring cell tumors, which are regarded as more aggressive and are more commonly found in young patients [8–10].

Whether patients received cancer-directed surgery was noted and was defined by the specific operation and SEER's "receipt of cancer-directed surgery" variable. Data regarding the type of radiation treatment, if any, were also collected.

Statistical Analyses

Statistical comparisons between groups were completed using the chi-square test of proportions or a two-sided Fisher's exact test when expected values were less than five. Survival data were compared using a two-tailed *t*-test of proportions. The 5-year cancer-specific survival analysis was computed using the Surveillance Research Program, National Cancer Institute SEER*Stat software (www.seer.cancer.gov/seerstat) version 4.2.3 (Information Management Services, Silver Spring, MD, USA). Patients were further analyzed based on age (20–40 years vs. 60–80 years), tumor location (i.e., "colon" as described above), and year of diagnosis (1991–1999). Survival was stratified by stage (AJCC stage I, II, II, or IV).

Multivariate Cox proportional hazards modeling was also performed to evaluate risk-adjusted outcomes. Independent covariates included for analysis were age group, gender, marital status at diagnosis, race, AJCC stage, grade, receipt of surgery, and receipt of radiation. All statistical analyses were completed using SAS version 8.02 (SAS Institute, Cary, NC, USA) or Stata Intercooled 7.0 (Stata, College Station, TX, USA). With $p < 0.05$, the differences were considered statistically significant.

Results

Demographics

A total of 47,791 patients with colon cancer were evaluated. The young group (20–40 years) included 1334 patients, and the older group (60–80 years) contained 46,457 patients. The mean age for the young group was 34.1 years and for the older group 70.8 years. Men comprised 52.1% of the young group and 51.5% of the older group (p = NS). Young patients were less likely to be married at the time of diagnosis, with 56.5% being married compared to 62.8% of the older group ($p < 0.001$).

The young group had a lower proportion of white patients and a higher proportion of black, Hispanic, and Asian patients, with 64.2% white in the young group compared to 81.2% in the older group ($p < 0.001$) (Table 1). The young group was comprised of 16.4% blacks, 6.5% Hispanics, and 7.4% Asians, in contrast to 9.0% blacks, 3.0% Hispanics, and 5.6% Asians in the older group ($p < 0.01$ for each).

Table 1. Patient demographics.

Parameter	Young (ages 20-40) (n = 1,334)	Older (ages 60-80) (n = 46,457)	p
Age (years)	34.1 ± 4.4	70.8 ± 5.4	
Gender (%)			
Male	52.1	51.5	NS
Female	47.9	48.5	NS
Race/ethnicity (%)			
White	64.2	81.2	< 0.001
Black	16.4	9.0	< 0.001
Hispanic	6.5	3.0	< 0.001
Asian	7.4	5.6	0.005
Other	5.5	1.2	< 0.001

Table 2. Tumor characteristics.

Characteristic	Young (ages 20–40) (n = 1334)	Older (ages 60–80) (n = 46,457)	p
AJCC stage (%)			
I	10.6	18.6	< 0.001
II	23.0	29.0	< 0.001
III	31.5	22.8	< 0.001
IV	24.5	17.3	< 0.001
Unstaged	10.4	12.3	NS
Grade (%)			
Well differentiated	7.2	9.7	0.002
Moderately differentiated	52.2	58.8	< 0.001
Poorly differentiated	27.3	17.2	< 0.001
Anaplastic	1.6	0.7	< 0.001
Unknown	11.7	13.6	NS
Histology (%)			
Mucinous	15.7	11.5	< 0.001
Signet ring cell	3.8	0.8	< 0.001

AJCC: American Joint Committee on Cancer.

Cancer-related Data

Young patients presented with fewer right-sided colon lesions (35.7% vs. 43.7%, $p < 0.001$) and more transverse colon lesions than their older counterparts, though the differences are probably not clinically relevant (11.2% vs. 9.1%, $p < 0.01$). There was no statistical difference between groups in terms of the frequency of left colon lesions (45.7% vs. 43.0%, p = NS).

Young patients presented with significantly less early-stage colon cancer than did the older group (i.e., less stage I and II disease) and significantly more stage III and IV disease (Table 2).

The young group had significantly worse histologic grades, presenting with fewer cases of well differentiated or moderately differentiated disease and more poorly differentiated or anaplastic tumors compared to their older counterparts. Young patients also had more mucinous and signet-ring tumors than the older group, with 15.7% of young patients having mucinous tumors compared to 11.5% of the older patients ($p < 0.001$) and 3.8% signet-ring cell tumors compared to 0.8% in the older group ($p < 0.001$) (Table 2).

Treatment, Survival, and Multivariate Cox Regression Analysis

Young patients were as likely to undergo cancer-directed surgical resection as their older counterparts, with 91.4% of young patients

Table 3. 5-Year cancer-specific survival.

Tumor	Young (ages 20-40)	Older (ages 60-80)	*p*
All colon tumors (%)	*n* = 1196	*n* = 35,837	
Overall	61.5	64.9	0.015
AJCC I	93.3	94.9	NS
AJCC II	88.6	82.7	0.01
AJCC III	58.9	57.2	NS
AJCC IV	18.1	6.2	< 0.001
Mucinous tumors (%)	*n* = 172	*n* = 4081	
Overall	50.5	60.7	0.007
AJCC I	[a]	92.4	[a]
AJCC II	75.5	83.4	NS
AJCC III	58.5	56.3	NS
AJCC IV	18.5	8.0	0.006
Signet ring tumors (%)	*n* = 46	*n* = 266	
Overall	3.7	34.9	< 0.001
AJCC I	[a]	100.0	[a]
AJCC II	[a]	54.3	[a]
AJCC III	27.8	43.2	NS
AJCC IV	17.7	2.8	0.013

[a]Insufficient sample size for analysis.

Table 4. Cox multivariate regression analysis.

Variable	Hazard ratio	*p*	95% Confidence interval
Young[a]	0.630	< 0.0001	0.574,0.691
AJCC II[b]	1.087	0.002	1.041,1.136
AJCC III[b]	1.935	< 0.0001	1.855,2.017
AJCC IV[b]	6.821	< 0.0001	6.550,7.103
Black[c]	1.195	< 0.0001	1.142,1.250
Hispanic[c]	0.951	0.2346	0.876,1.033
Asian[c]	0.830	< 0.0001	0.777,0.885
Other race[c]	0.771	0.0005	0.666,0.892
Male[d]	1.095	< 0.0001	1.065,1.126
Low grade[e]	0.741	< 0.0001	0.719,0.763
Underwent irradiation[f]	1.016	0.6582	0.946,1.092
Underwent surgery[g]	0.302	< 0.0001	0.289,0.316

[a]Reference group is older.
[b]Reference group is AJCC I.
[c]Reference group is white.
[d]Reference group is female.
[e]Reference group is high grade.
[f]Reference group did not undergo irradiation.
[g]Reference group did not undergo surgery.

and 91.2% of older patients having cancer-directed surgery (p = NS). Similar findings were seen specifically for surgery for stage I, II, and III disease (99.2–99.7% underwent surgery). However, older patients with stage IV disease had surgery significantly less often than young patients (74.6% vs. 83.2%, $p < 0.001$).

Univariate analysis revealed that overall 5-year cancer-specific survival was significantly worse for the young group than for the older group (61.5% vs. 64.9%, $p = 0.015$). However, the 5-year stage-specific survival was similar for stage I disease (93.3% vs. 94.9%, p = NS). Survival was significantly better for young patients with stage II disease (88.6% vs. 82.7%, $p = 0.01$), equal for stage III disease (58.9% vs. 57.2%, p = NS), and significantly better for stage IV disease (18.1% vs. 6.2%, $p < 0.001$) (Table 3). Specifically for mucinous and signet-ring tumors, the overall and stage-specific 5-year survivals were worse for the young group, except for those with stage IV disease (Table 3).

To support these findings, multivariate Cox regression analysis revealed that when controlling for tumor stage along with patient demographics, tumor characteristics, and treatment, young patients had a lower hazard of dying (hazard ratio 0.630; 95% confidence interval 0.574, 0.691; $p < 0.0001$) (Table 4).

Discussion

Three percent of patients diagnosed with colon cancer from 1991 to 1999 were "young" (20–40 years). Therefore of the 107,300 new cases diagnosed in 2002, an estimated 3200 would occur in patients between the ages of 20 and 40. This number is similar to the annual burden of anal cancer or acute lymphocytic leukemia for all ages [1].

Previous studies have reported a wide range in the percentage of colorectal patients who fall into the "young" (< 40 years) age group, ranging from 0.4% to 35.6% [11–22]. The few studies that focused specifically on colon cancer cited percentages ranging between 3.2% and 6.3% [15, 23]. This discrepancy likely reflects the inherent variability in studies from single centers, which are often referral centers and tend to treat more individuals with advanced disease. The potentially skewed sample of patients described in these studies is likely to provide tumor characteristics and survival findings that may not be generalizable to the population as a whole. Our study, which used nationally representative data, is in agreement with the literature reporting that young patients tend to present with later-stage disease and higher-grade lesions. In contrast, however, we have found young patients to have similar if not better 5-year stage-specific survival than their older counterparts.

With regard to stage, the current study found 56% of young patients presented with stage III or IV disease compared to 40% in the older group. This finding is somewhat lower than that reported by others, including Adkins et al., who found that 77.6% of young patients present with Dukes' C or D tumors [15]. Similarly for tumor grade, we found that 28.9% of young patients presented with poorly differentiated or anaplastic tumors compared to 17.9% in the older population ($p < 0.01$). This population-based finding more clearly defines the reported array of young patients with poorly differentiated or anaplastic tumors (8.7–54.2%). [24, 25]

One of the more important histologic factors cited in the literature is the disproportionately higher rate of mucinous and signet-ring tumors in the young group. We found that 16% of young patients presented with mucinous tumors and 4% with signet ring tumors. This finding also narrows the wide range seen in the literature (i.e., 3–69% for mucinous lesions and 8–41% for signet ring tumors) [8–10].

Probably the most significant finding of the current analysis is the 5-year survival rates. We found that overall 5-year cancer-specific survival for young patients is poorer than for older patients (62% vs. 65%), but stage for stage young patients have similar, and in some instances better, overall 5-year survival. We found that young patients had 93% five-year survival for stage I disease, 89% for stage II disease, 59% for stage III, and 18% for stage IV compared to 95%, 83%, 57%, and 6%, respectively, for the older patients. This is in contrast to what has previously been reported in most of the literature, which has consistently suggested that young patients have poorer 5-year survivals both overall and stage for stage. The two largest studies of colorectal cancer in the young that evaluated survival reported 32% and 33% overall 5-year survival [4, 13]. Though not cause-specific, these numbers are still significantly

lower than our finding of 61.5%. Furthermore, the range of cited overall 5-year survivals (0–60%) is extremely wide and lower than what we found [16, 26].

Why younger patients have better survival for stage II and IV lesions but equivalent survival for stage I and III tumors is unknown. One hypothesis concerns the use of adjuvant chemotherapy. In the 1990 National Institutes of Health Consensus Guidelines for the treatment of colorectal cancers, explicit guidelines were published recommending surgical treatment alone for stage I disease and surgical plus adjuvant chemotherapy for stage III disease [27]. In this regard, it is probable that most patients (young and older) received uniform treatment for these stages. However, in the clinical world, adjuvant treatment for stage II and IV disease is much less uniform, and it is possible that a higher proportion of young patients with stage II and IV diseases received chemotherapy than older patients with similar stage disease. Unfortunately, SEER does not contain information regarding receipt of chemotherapy, and so we were unable to evaluate differences in chemotherapeutic treatments or control for it in the multivariate analysis. Future studies should evaluate these topics, potentially linking SEER records with claims data, to determine if these hypotheses play a role in improved survival for young patients.

Although this is the largest population-based study to date that has evaluated colon cancer in a young versus older population, there are potential limitations with the results. First, although the SEER registry maintains stringent quality control measures to prevent coding errors and is regarded as one of the best population-based databases available, possible miscoding and inaccurate data may be present. SEER does, however, uphold several quality control measures to ensure accuracy; and it maintains the highest level of certification of data quality and completeness, as reported by the North American Association of Central Cancer Registries [28]. SEER adheres to strict quality assessment measures by checking the accuracy of sample cases by reabstracting data from medical records each year. The completeness of each case has been reported as approximately 98%. [29]

Second, the registry does not contain all clinically relevant data. For example, information such as family history, predisposing factors (e.g., personal medical history), presenting symptoms, time from onset of symptoms to diagnosis (i.e., if there was a "delay in diagnosis"), and receipt of chemotherapy is not available. It is possible that our findings that young colon cancer patients have similar or better survivals than their older counterparts may be affected by a potentially higher proportion of young patients with familial colon cancer syndromes. We were unable to evaluate this point specifically as this information is not available in SEER.

Despite these potential limitations, there are many advantages to the population-based SEER registry. First, we were able to analyze 47,791 patients with colon cancer over a 9-year period, which is a much larger sample size than any other comparable study. Second, SEER is nationally representative, as it is a cross-sectional sample representing 14% of the U.S. population, which is ethnically and socioeconomically diverse [30]. As such, these finding are easily generalizable to the overall U.S. population.

Conclusions

We have previously reported that there has been an increase in the incidence of colon cancer in the young [7]. The current study uses a national, population-based data sample to show that young patients present with later-stage and higher-grade disease. Contrary to prior reports, younger patients appear to have similar or better stage-specific survival than older patients. Although the overall prevalence of colon cancer in young patients is low, health care providers should have a heightened awareness when caring for this population. This is particularly important with regard to screening for potential familial colon cancer syndromes, as excellent modalities exist to diagnose and treat this cancer.

Résumé. Des études antérieures concernant le cancer colique ont mis l'accent sur l'incidence croissante chez les individus jeunes: elles suggèrent que ces cancers sont plus agressifs et que la survie à 5 ans est moins bonne. Notre étude fait appel à un registre basé sur les données nationales de population afin d'analyser la présentation et l'évolution des patients jeunes porteurs de cancer colique comparées aux patients plus âgés. Les dossiers des patients porteurs de cancer du côlon ont été obtenus à partir de la banque de données nationale sur le cancer «SEER» (Surveillance, Epidemiology, and End Results) (1991–1999). Deux cohortes, basées sur l'âge au moment du diagnostic (20–40 ans, $n = 1334$ vs. 60-80 ans, $n = 46,457$) ont été comparées en ce qui concerne les caractéristiques des patients, des tumeurs, le traitement et la survie en rapport avec la maladie à 5 ans. Une analyse multivariée selon le modèle de Cox a été utilisée pour trouver les facteurs prédictifs de survie. Dans le groupe de patients plus jeunes, la proportion de personnes de race noire et des hispaniques était plus élevée par rapport au groupe plus âgé ($p < 0.001$). Il y avait parmi les plus jeunes moins de patients aux stades I et II de la maladie, plus de patients aux stades III et IV ($p < 0.001$) et porteurs de cancer indifférencié ou anaplasiques ($p < 0.001$). La survie à 5 ans, stage spécifique, était similaire pour les stades I et III (p = NS), mais meilleure de façon statistiquement significative pour les patients plus jeunes, porteurs de maladie des stades II et IV ($p < 0.01$). Grâce au registre représentatif présenté ici, nous avons trouvé que les patients jeunes, porteurs de cancer colique, ont une tendance à se présenter plus tardivement et avec des tumeurs de grade plus élevé. Cependant, comparée à la survie des patients plus âgés, leur survie à 5 ans en ce qui concerne leur maladie était équivalente ou meilleure. Ces données basées sur la population globale sont en contradiction avec les données antérieures de provenance mono-institutionnelle.

Resumen. Estudios previos sugerían un incremento de la frecuencia del cáncer de colon en pacientes jóvenes, así como una mayor agresividad tumoral con la consiguiente disminución de la supervivencia a 5 años. Nuestro trabajo se basa en los datos obtenidos de un registro de cáncer que incluye a toda la población nacional. Se estudia la incidencia del cáncer de colon y los resultados del tratamiento en jóvenes frente a pacientes añosos. Los datos de pacientes con cáncer de colon se obtuvieron de los protocolos sobre vigilancia, epidemiología y resultados finales (SEER) procedentes del Registro Nacional del Cáncer entre los años 1991–1999. De acuerdo con la edad del paciente en el momento de efectuar el diagnóstico se elaboraron dos cohortes (20–40 años, $n = 1334$ frente a 60–80 años, $n = 46,457$) que se compararon entre sí por lo que a las características del tumor, tratamiento y supervivencia a los cinco años se refiere. Aplicamos la regresión multivariante de Cox para identificar los factores pronósticos por lo que a la supervivencia atañe. En el grupo de pacientes jóvenes se registró un mayor número de negros e hispanos que en el grupo de pacientes añosos ($p < 0.001$). En pacientes jóvenes los estadios I y II fueron menos frecuentes que los III y IV ($p < 0.001$), el grado de agresividad tumoral (poco diferenciados o anaplásícos) también fue mayor en dicho grupo ($p < 0.001$). Sin embargo, al comparar la supervivencia a los 5 años entre ambos grupos para los estadio I y III no se constataron diferencias estadísticas (p = NS) pero en pacientes jóvenes con estadios II y IV la supervivencia fue significativamente mayor ($p < 0.01$). Utilizando el Registro Nacional del Cáncer, comprobamos que los pacientes jóvenes con cáncer de colon tienden a padecer tumores con estadificación más alta y con mayor grado de malignidad. Sin embargo, su supervivencia a los 5 años es igual o menor que la registrada en pacientes añosos. Estos hallazgos basados en los datos obtenidos del Registro Nacional del Cáncer contradicen los resultados previamente publicados basados en las casuísticas de centros hospitalarios aislados.

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