

Increasing Incidence of Adenocarcinomas and Carcinoid Tumors of the Small Intestine in Adults

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Abstract

Malignant neoplasms of the small intestine are relatively rare and have received little study. We report on trends in the age-adjusted, sex-, and race-specific incidence rates of adenocarcinomas and carcinoid tumors of the small intestine in the United States from 1973 through 1991. Data were derived from the Surveillance, Epidemiology, and End Results Program of the National Cancer Institute. There were statistically significant increases in the incidence rates of both adenocarcinomas and carcinoid tumors during the time frame of the study. Rates increased most dramatically in black males, with 2- and 4-fold increases in adenocarcinomas and carcinoid tumors, respectively. The only rates that remained relatively unchanged were those of adenocarcinoma among white females. It remains to be determined if changing environmental factors are important causes of these observed trends. If environmental factors are involved in the etiology of small intestine cancers, analytic studies conducted while the disease is increasing in incidence may provide useful insights.

Introduction

Malignant neoplasms of the small intestine are rare relative to cancers of other gastrointestinal sites such as esophagus, stomach, colon, and rectum. The American Cancer Society estimates that there will be 4600 newly diagnosed cases of cancer of the small intestine in the United States during 1995 (1). A recent study estimated that adenocarcinomas and carcinoid tumors account for approximately 77.5% of these cancers (2). Thus, adenocarcinomas and carcinoid tumors of the small intestine will comprise approximately 0.3% of all newly diagnosed cancers in 1995.

Perhaps because of their rare nature, these cancers have received little attention in the scientific literature. The purpose of this analysis is to present data on trends over time in the incidence rates of adenocarcinomas and carcinoid tumors of the small intestine in the United States.

Materials and Methods

Data for this analysis were obtained from the public use tape of the SEER² program of the National Cancer Institute (3). The backbone of the SEER program is a set of geographically defined, population-based central cancer registries. Information was included from nine SEER registries covering the states of Connecticut, Iowa, New Mexico, Utah, and Hawaii and the metropolitan areas of Atlanta (GA), Detroit (MI), San Francisco-Oakland (CA), and Seattle (WA). These registries cover approximately 10% of the United States' population. Cases included were restricted to those patients for whom cancers were: (a) primary neoplasms of the small intestine [ICD-O (4) topography classification of C17.0-C17.9]; (b) adenocarcinoma (ICD-O morphological classification of 8140–8231 or 8246–8381) or carcinoid tumor (ICD-O morphology classification of 8240–8245); (c) malignant (fifth digit of morphology code = 3); (d) ≥ 20 years of age at diagnosis; and (e) newly diagnosed from January 1973 through December 1991.

Age-adjusted, gender-specific incidence rates were computed separately for blacks and whites. Both numerator and denominator data were taken directly from SEER information. Denominator data were derived from interpolations based on the 1970, 1980, and 1990 censuses and were computed for the SEER Program by the United States Bureau of the Census. Rates were age adjusted to the 1970 United States standard million population using the direct method. Unless otherwise specified, all rates are expressed per 1,000,000 population/year. Poisson regression was used to evaluate whether over time the trends in incidence rates were likely to have occurred by chance (5).

Results

A total of 3292 cases were identified, of which 1609 (48.9%) were adenocarcinomas and 1683 (51.1%) were carcinoid tumors. Table 1 shows the number and proportion of cases by selected demographic and clinical characteristics. More than 99% of the diagnoses were confirmed microscopically. Adenocarcinomas were similar to carcinoid tumors in relation to race, gender, age, and stage at diagnosis. Adenocarcinomas proportionately were more likely to be located in the duodenum (48.3%) and jejunum (23.4%), whereas carcinoid tumors were more likely to be found in the ileum (56.5%). In addition, carcinoid tumors were more likely than adenocarcinomas to be coded as site NOS. Although the proportion of NOS adenocarcinomas remained fairly constant over time, averaging 11.3% during 1973–1977 and 11.1% during 1987–1991, the propor-

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² The abbreviations used are: SEER, Surveillance, Epidemiology, and End Results program; NOS, not otherwise specified; AAPI, average annual percentage increase; CI, confidence interval.

Table 1 Number of cases of adenocarcinoma and carcinoid tumors of the small intestine among the population ≥ 20 years of age by selected demographic and clinical characteristics for nine SEER areas, 1973–1991

	Adenocarcinoma		Carcinoid	
	<i>n</i>	%	<i>n</i>	%
Total	1609	100.0	1683	100.0
Race				
White	1353	84.2	1450	86.5
Black	195	12.1	194	11.6
Other	58	3.6	33	2.0
Unknown	3		6	
Gender				
Male	842	52.3	888	52.8
Female	767	47.7	795	47.2
Age (yrs)				
20–39	63	3.9	61	3.6
40–59	432	26.8	474	28.2
60–79	877	54.5	928	55.1
80+	237	14.7	220	13.1
Yr of diagnosis				
1973–1975	191	11.9	152	9.0
1976–1978	208	12.9	176	10.5
1979–1981	199	12.4	232	13.8
1982–1984	264	16.4	233	13.8
1985–1987	301	18.7	347	20.6
1988–1991	446	27.7	543	32.3
Microscopic confirmation				
Yes	1597	99.3	1674	99.5
No	12	0.7	9	0.5
Stage				
Local	383	25.8	421	26.2
Regional	642	43.3	658	40.9
Distant	457	30.8	528	32.9
Unknown	127		76	
Primary site				
Duodenum	777	48.3	114	6.8
Jejunum	376	23.4	125	7.4
Ileum	251	15.6	951	56.5
Meckel's diverticulum	8	0.5	24	1.4
Overlapping lesion	25	1.6	15	0.9
NOS	172	10.7	454	27.0

tion of NOS carcinoid tumors rose from 17.6% during 1973–1977 to 29.1% during 1987–1991.

Table 2 illustrates the annual age-adjusted incidence rates for adenocarcinomas and carcinoid tumors for white males and females and for black males and females. The rate of adenocarcinomas rose substantially among black males from an average of 8.2 in 1973–1977 to 16.0 in 1987–1991, whereas the corresponding rates among black females rose from an average of 5.1 in 1973–1977 to 15.7 in 1987–1991. The rate of adenocarcinomas rose slightly among white males (6.2 in 1973–1977 to 8.5 in 1987–1991) and remained relatively steady among white females (4.8 in 1973–1977 to 5.1 in 1987–1991). The AAPI in rates for adenocarcinomas estimated from the Poisson regression are shown in Table 3. The rates of adenocarcinomas increased significantly over time in both blacks and whites, although the AAPI for blacks (6.4%) was higher than that for whites (1.4%). Additional models including gender were evaluated (data not shown) but did not appreciably affect the AAPI after controlling for age. As mentioned previously, almost one-half (48.3%) of the adenocarcinomas were located in the duodenum. We found no difference in trends between rates for

all adenocarcinomas and rates for adenocarcinomas restricted to the duodenum (data not shown).

The incidence rate of carcinoid tumors increased almost 4-fold among black males, from an average of 6.0 in 1973–1977 to 23.3 in 1987–1991, and over 2-fold among white males, from 5.0 in 1973–1977 to 10.4 in 1987–1991 (Table 2). The carcinoid tumor incidence rate for white females rose from an average of 4.4 in 1973–1977 to 7.2 in 1987–1991, whereas the rate for black females rose from 6.0 in 1973–1977 to 8.5 in 1987–1991. The AAPI for carcinoid tumors among whites was similar for males (5.5%; 95% CI = 4.0–6.9%) and females (4.2%; 95% CI = 2.7–5.7%). However, the AAPI among blacks differed between males and females, with males showing a relatively high AAPI of 8.3% (95% CI = 4.3–12.4%) compared to females (2.8%; 95% CI = –1.5–7.4%). In black males, the AAPI appeared to increase substantially after 1984, but this increase was not statistically significant ($P = 0.313$). More than one-half (56.5%) of carcinoid tumors were located in the ileum. In general, the trends were similar between rates for all carcinoid tumors and the rates for carcinoid tumors restricted to the ileum (data not shown).

Discussion

We report a statistically significant increase in the incidence rates of both adenocarcinomas and carcinoid tumors of the small intestine from 1973 to 1991 in the United States. Although an increase was observed among both blacks and whites, it appears that the rates have increased to a greater extent for blacks. In fact, rates have increased most dramatically over time in black males, with a 2-fold and a 4-fold increase in the rates of adenocarcinoma and carcinoid tumors, respectively. The only rates that have remained relatively unchanged are those of adenocarcinomas among white females. Potential reasons for these increases remain open to speculation. We are unaware of any new and/or major changes in the methods used in diagnosing cancers of the small intestine that would be applied more so to black males than to white females.

Utilization of information from SEER has several advantages, including the population-based nature of case identification and the uniformity of data collection procedures. Perhaps the most important limitation to the use of these data for this analysis is the potential for missing and/or misclassified data. For example, the proportion of carcinoid tumors that were coded as site NOS increased throughout the time frame of the study, despite the fact that almost all of these tumors were confirmed microscopically.

Almost nothing is known about the etiology of cancers of the small intestine. This may be due, in some part, to the rarity of malignant tumors in the small intestine compared to other gastrointestinal sites, such as the colon and stomach. Several mechanisms have been suggested to account for the rare nature of these tumors, including the decreased transit time of contents through the small intestine (relative to the colon), the fluid nature of the contents within the small intestine (relative to the colon), and/or an efficient repair mechanism for small intestine epithelial cells (6, 7). Small intestine cancer is often diagnosed late in the course of disease or found incidentally at the time of diagnostic evaluation for other gastrointestinal disorders. This may be especially true for carcinoid tumors, for which resection is an important aspect of treatment for symptom control regardless if metastasis has or has not occurred.

Table 2 Annual age-adjusted, race-, and gender-specific rates per million for adenocarcinomas and carcinoid tumors of the small intestine among the population ≥ 20 years of age for nine SEER areas, 1973–1991

Yr	Adenocarcinoma				Carcinoid tumors			
	White		Black		White		Black	
	Male	Female	Male	Female	Male	Female	Male	Female
1973	5.6	5.7	18.7	13.5	3.2	2.3	0	6.1
1974	6.0	5.4	3.2	5.9	4.5	5.1	14.4	7.0
1975	6.8	4.4	7.7	0	6.0	5.4	2.1	8.2
1976	6.5	5.1	5.2	2.0	4.9	3.4	6.3	4.5
1977	6.3	3.6	6.0	3.9	6.2	5.7	7.4	4.0
1978	6.8	5.4	9.3	5.4	5.2	2.9	6.7	1.8
1979	4.9	3.0	5.3	3.6	7.8	4.3	11.5	5.9
1980	5.4	4.8	13.7	7.7	6.2	6.4	12.1	3.7
1981	6.2	4.4	4.3	12.6	4.6	5.2	12.3	7.4
1982	6.2	4.3	6.3	10.3	7.5	3.9	13.0	10.6
1983	8.8	6.1	15.3	6.5	5.8	4.1	5.7	5.5
1984	6.2	4.7	6.6	11.9	7.7	4.1	8.5	8.8
1985	8.2	5.3	16.7	2.6	7.5	4.4	8.2	7.4
1986	8.3	5.0	6.6	8.0	10.8	7.0	24.5	7.4
1987	9.3	4.6	23.4	21.3	10.1	7.7	25.0	5.3
1988	8.8	5.5	14.8	12.5	9.8	7.5	16.5	12.0
1989	6.9	4.6	10.9	14.1	11.3	8.5	34.0	10.6
1990	7.6	4.0	15.3	13.8	9.5	5.7	18.3	7.3
1991	9.9	6.6	15.6	17.0	11.5	6.5	22.3	7.1

Table 3 Age-adjusted incidence rates and AAPI in incidence rates of adenocarcinoma and carcinoid tumors of the small intestine among the population ≥ 20 years of age for nine SEER areas, 1973–1991

Type of neoplasm	Race	Rate/million	AAPI ^a	95% CI	P value ^b
Adenocarcinomas	Whites	5.7	1.4%	0.4–2.4%	0.0057
	Blacks	7.5	6.4%	3.5–9.4%	<0.0001
Carcinoid tumors	Whites	6.1	4.5%	3.5–5.5%	<0.0001
	Blacks	7.5	5.9%	2.9–8.9%	<0.0001

^a Controlling for age at diagnosis.

^b Likelihood ratio test for trend.

Most reports, including this study, tend to be descriptive in nature (2, 7–10). Although such studies can be important and provide useful leads in the search for etiological clues, analytic studies are needed to provide more detailed information on potential risk factors. Two case-control studies of cancers of the small intestine have reported increased risk among consumers of red meats and salt-cured/smoked foods (11) and individuals with Crohn's disease (12). These studies differed considerably in their findings related to alcohol and tobacco consumption. Chen *et al.* (12) reported odds ratios of 4.6 (95% CI = 1.0–20.7) for adenocarcinoma and 4.2 (95% CI = 0.8–22.4) for carcinoid tumors among cigarette smokers compared to nonsmokers (controlling for age, gender, and alcohol consumption). In addition, they reported an odds ratio of 4.0 (95% CI = 1.0–15.9) for adenocarcinomas and 3.1 (95% CI = 0.7–13.9) for carcinoid tumors among drinkers compared to nondrinkers. Chow *et al.* (11) found no increased risk in either smokers or drinkers. These differences are difficult to reconcile, although variations in case eligibility requirements and sample size may be contributing factors. The study by Chen *et al.* (12) was based on 36 incident cases of all races and included histology specific analyses, whereas the study by Chow *et al.* (11) was based on 430 white cases who had died as a result of cancer of the small intestine and did not include any histology specific analyses. In addition, the small number of cases in the study

by Chen *et al.* (12) is reflected in the relatively wide CIs for their risk estimates.

We suggest that more detailed analytic studies of cancers of the small intestine are needed and would be useful for two reasons: (a) additional studies should help to resolve the discrepant findings associated with tobacco and alcohol consumption; and (b) if there are environmental factors involved in the etiology of cancers of the small intestine, analytic studies that are conducted while the disease is increasing in incidence may provide useful insights.

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