Subsite-Specific Colorectal Cancer Incidence Rates and Stage Distributions among Asians and Pacific Islanders in the United States, 1995 to 1999

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Abstract

Objective: This study examined subsite-specific colorectal cancer incidence rates and stage distributions for Asians and Pacific Islanders (API) and compared the API data with data for Whites and African Americans. Methods: Data included 336,798 invasive colorectal cancer incident cases for 1995 to 1999 from 23 population-based central cancer registries, representing about two thirds of API population in the United States. Age-adjusted rates, using the 2000 U.S. standard population, and age-specific rates and stage distributions were computed by anatomic subsite, race, and gender. All rates were expressed per 100,000. SEs and rate ratios were calculated for rate comparison. A significance level of 0.05 was used for all analyses. Results: Overall, age-adjusted colorectal cancer incidence rates were significantly lower in API than in Whites and African Americans across anatomic subsites, particularly for proximal colon cancer in which rates were 40% to 50% lower in API males and females. Exception to this pattern was the significantly (10%) higher rectal cancer incidence rate in API males than in African American males. The incidence patterns by anatomic subsite within API differed from those of Whites and African Americans. Among API, the rate of rectal cancer (19.2 per 100,000) was significantly higher than the rates of proximal (15.2 per 100,000) and distal (17.7 per 100,000) colon cancers in males, with little variations in rates across anatomic subsites in females. In contrast, among White and African American males and females, proximal colon cancer rates were over 25% higher than the rates of distal colon and rectal cancers. Increases in age-specific rates with advancing age were more striking for proximal colon cancer than for distal colon and rectal cancers in Whites and African Americans, while age-specific rates were very similar for different subsites in API with parallel increases with advancing age, especially in API males. Similar to Whites and African Americans, in API, proximal colon cancers (32% to 35%) were also less likely to be diagnosed with localized stage compared with distal colon (38% to 42%) and rectal (44% to 52%) cancers. Conclusion: The patterns of subsite-specific colorectal cancer incidence in API, especially API males, differ from those of Whites and African Americans. Similar to Whites and African Americans, lower percentage of localized disease in API for proximal colon cancer than for distal colon and rectal cancers was also observed. (Cancer Epidemiol Biomarkers Prev 2004;13(7):1215–22)

Introduction

Previous studies have suggested that incidence rates of subsite-specific colorectal cancer vary by race, gender, and age group (1-4). It has also been noted that rate ratios of proximal to distal colorectal cancer increase with advancing age and that females are at increased risk for proximal cancer (1, 2, 4, 5). However, most studies on this topic include only White and African American race groups. Data on subsite-specific colorectal cancer incidence are scarce for Asians and Pacific Islanders (API) in the United States, although they represent one of the nation's fastest growing minorities (6). We examined subsite-specific cancer incidence rates and stage distributions for API and compared the API data with data for Whites and African Americans using a large aggregated cancer incidence database from 23 population-based cancer registries in the United States.

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Materials and Methods

Study Population. Cancer incidence data for the years 1995 to 1999 were obtained from the North American Association of Central Cancer Registries (NAACCR) including 23 population-based central cancer registries that consented to contribute data for this study. They were California, Colorado, Connecticut, Atlanta (Georgia), Hawaii, Iowa, Idaho, Illinois, Kentucky, Louisiana,

Michigan, Minnesota, Nebraska, New Jersey, New Mexico, North Carolina, Pennsylvania, Rhode Island, Utah, Seattle/Puget Sound (Washington), West Virginia, Wisconsin, and Wyoming. These states and metropolitan areas cover ~47% of the U.S. population, 47% of Whites, 40% of African Americans, and 64% of API (7, 8).

Data from each of these registries have passed strict criteria for completeness of case ascertainment (90% or higher), nonduplication of reported cancer cases (duplicate cases did not exceed 2 per thousand), internal consistency among data items defined by the NAACCR EDITS metafile, low percentage of death certificate–only cases (<5%), and low percentages of cases with missing/unknown race (<5% unknown), gender, and age (<3% unknown; ref. 9). Only data for Whites, African Americans, and API were included in this study because of uncertainty about the quality of data on other race groups such as American Indians/Alaska Natives. Information on specific race in the registries' data is derived from medical records, coded according to standard codes (10), and grouped into standard race categories in compliance with federal agency standards for the years that the study data were collected (11). The API category includes Chinese, Japanese, Filipino, Hawaiian, Korean, Asian Indian-Pakistani, Vietnamese, Laotian, Hmong, Kampuchean, Thai, Micronesian-not otherwise specified (NOS), Chamorran, Guamanian-NOS, Polynesian-NOS, Tahitian, Samoan, Tongan, Melanesian-NOS, Fiji Islander, New Guinean, and Other API-NOS, Oriental-NOS, and Pacific Islander-NOS. The reason why we combined all API subcategories into one group was that population data for subgroups of the API categories were not available. Population estimates for 1995 to 1999 were obtained from the Surveillance, Epidemiology, and End Results program based on the U.S. Bureau of Census population estimates for these years (12).

This study included incident cases of invasive primary colorectal cancers coded according to the *International Classification of Diseases for Oncology, Second Edition* topography (site) codes C18.0 to C18.9, C19.9, C20.9, and C26.0 (13). Malignant lymphomas were excluded. Colorectal cancers were grouped into three major anatomic subsites: proximal colon, distal colon, and rectum. Proximal colon included the cecum (C18.0), ascending colon (C18.2), hepatic flexure (C18.3), transverse colon (C18.4), and splenic flexure (C18.5). Distal colon consisted of the descending colon (C18.6) and sigmoid colon (C18.7). Rectum included rectosigmoid junction (C19.9) and rectum-NOS (C20.9). Cancers of the appendix (C18.1), colon-NOS (C18.9), overlapping subsites (C18.8), and intestinal tract-NOS (C26.0) accounted for 6.0% of all colorectal cancer cases in the study data file. These cancer cases were included in the statistics for the total colon and rectum but not for the specific anatomic subsites.

Colorectal cancer cases were staged using the Surveillance, Epidemiology, and End Results summary staging system (14). We collapsed the subcategories of regional stage as specified in the summary staging system into one category; this resulted in four major stage groups: localized (confined to colon or rectum), regional (extension to adjacent tissues or regional lymph nodes), distant (metastasis to other areas of the body), and unknown stage. Overall, cases staged as ''unknown'' accounted for ~8% of colorectal cancer cases. Stage distributions in this study were calculated based on known stage cases. Because recommended screening for individuals at average risk for colorectal cancer begins at age 50, we focused on stage data for patients ≥50 years old. Those ≤50 years old only accounted for 7% of all colorectal cancer cases in the study data file. Because summary stage data for California were not available in the study data file, with the exception of metropolitan Los Angeles and the Great Bay Area, data from these two metropolitan areas were the only California data included in the stage distributions.

Statistical Analysis. Average annual age-specific and age-adjusted incidence rates per 100,000 were computed by anatomic subsite, race, and gender. The 2000 U.S. standard population was used to obtain age-adjusted rates. SEs and incidence rate ratios were calculated for rate comparisons (15). The stage distributions were examined by anatomic subsite, race, gender, and age group (<50 and >50 years). A significance level of 0.05 (two tailed) was used for all analyses. Counts and rates were suppressed when <16 cases were in individual cells.

Results

This study included a total of 336,798 eligible invasive colorectal cancer cases diagnosed in 1995 to 1999. There were 297,851 Whites (88.4%), 28,354 African Americans (8.4%), and 10,593 API (3.1%). Overall, the age-adjusted (2000 U.S. standard) colorectal cancer incidence rate for both genders combined among API (44.9 per 100,000) was 19.8% lower than that among Whites (56.0 per 100,000) and 27.3% lower than that among African Americans (61.8 per 100,000); these differences were statistically significant.

Subsite-Specific, Age-Adjusted Rates by Race and Gender. Age-adjusted incidence rates of proximal colon cancer were significantly higher than the rates of distal colon cancer and rectal cancer in Whites and African Americans for both males and females and API females (Tables 1 and 2). In contrast, the pattern for API males was reversed. For API males, the rate of rectal cancer was 26% higher than the rate of proximal colon cancer and ~8% higher (not significant) than the rate of distal colon cancer.

For proximal colon cancer, API had the lowest incidence rates of the three race groups (Tables 1 and 2). The rate for API males was 40% lower than the rate for White males and 50% lower than the rate for African American males. For females, the rate in API was 38% lower than the rate in Whites and 48% lower than the rate in African Americans. The racial differences in the rates were much smaller for distal colon and rectal cancer than for proximal colon cancer. For distal colon cancer, the rate in API males was about the same as the rate in White males and 7% lower than the rate in African American males. The rate in API females was about the same as the rate in White females and significantly (13%) lower than the rate in African American females. For rectal cancer, the rate in API males was about the same as the rate in White males and significantly (10%) higher than the rate

Table 1. Age-adjusted (2000 U.S.) incidence rates* and rate ratios of colorectal cancer by race and anatomic subsite, selected areas in the United States,† 1995 to 1999, males

Anatomic Subsite	Age-Adjusted Rates			Rate Ratios (95% Confidence Intervals)	
	API	Whites	Blacks	API/Whites	API/Blacks
Colon and rectum‡	54.2	67.2	72.2	0.81 (0.79-0.83)§	0.75 (0.73-0.78)§
Proximal colon‖	15.2	25.2	30.2	0.60 (0.58-0.63)§	0.50 (0.48-0.53)§
Cecum (C18.0)	4.9	9.9	11.3	0.49 (0.46-0.52)§	0.43 (0.39-0.47)§
Ascending (C18.2)	4.3	7.1	8.4	0.61 (0.56-0.66)§	0.51 (0.47-0.56)§
Transverse plus two flexures (C18.3 to C18.5)	5.9	8.2	10.6	0.72 (0.66-0.79)§	0.56 (0.51-0.62)§
Distal colon	17.7	18.0	19.1	0.98 (0.93-1.03)	0.93 (0.88-0.98)§
Descending (C18.6)	3.0	3.0	4.4	1.00	0.68 (0.58-0.79)§
Sigmoid colon (C18.7)	14.7	15.1	14.7	0.97 (0.91-1.03)	1.00
Rectum	19.2	20.1	17.4	0.96 (0.93-1.00)	1.10 (1.04-1.16)§
Rectosigmoid junction (C19.9)	6.1	6.4	5.5	0.95 (0.88-1.02)	1.11 (1.01-1.22)§
Rectum (C20.9)	13.2	13.7	11.9	0.96 (0.90-1.03)	1.11 (1.03-1.20)§

*Rates are per 100,000 and age adjusted to the 2000 U.S. population standard.
† Source: NAACCR 1995 to 2000 analytic data file, including California, Colorado, Connecticut, Atlanta (Georgia), Hawaii, Iowa, Idaho, Illinois, Kentucky, Louisiana, Michigan, Minnesota, Nebraska, New Jersey, New Mexico, North Carolina, Pennsylvania, Rhode Island, Utah, Seattle/Puget Sound (Washington), West Virginia, Wisconsin, and Wyoming.
‡ *International Classification of Diseases for Oncology, Second Edition* topograph codes are C18.0 to C18.9, C19.9, C20.9, and C26.0. Lymphomas were excluded.
§The rate ratio is significantly different ($P < 0.05$) from 1.00.
‖Appendiceal cancers were not included in this group.

in African American males. The rate in API females was significantly (~12%) lower than the rates in White females and significantly (9%) lower than in African American females.

Incidence rates increased with advancing age for all colorectal cancer subsites. The upward trends of age-specific rates were more striking for proximal colon cancer than for distal colon and rectal cancers in Whites and African Americans for both males and females (Fig. 1). In contrast, the trends of age-specific incidence rates were very similar for different subsites in API males. For API females, although the rates of proximal colon cancer were higher than for distal colon and rectal cancers in the older age groups, the difference in the rates between proximal colon cancer and distal colon and rectal cancers in each of the age groups was much smaller than in Whites and African Americans.

Stage and Anatomic Subsites by Race, Gender, and Age Group. For all race and gender groups, cancer in the proximal colon was less likely to be diagnosed at a localized stage than cancers in the distal colon and rectum (Tables 3 and 4). This pattern was observed among those <50 years old and those ≥50 years old. However, patients ≥50 years old were more likely to be diagnosed with localized cancers than their younger counterparts (data not shown). For patients ≥50 years old, about one third were staged as localized for proximal colon cancer; in contrast, ~37% to 42% of distal colon cancer and 40% to 51% of rectal cancer were staged as localized.

Table 2. Age-adjusted (2000 U.S.) incidence rates* and rate ratios of colorectal cancer by race and anatomic subsite, selected areas in the United States,† 1995 to 1999, females

Anatomic Subsite	Age-Adjusted Rates			Rate Ratios (95% Confidence Intervals)	
	API	Whites	Blacks	API/Whites	API/Blacks
Colon and rectum‡	37.6	47.8	54.9	0.79 (0.77-0.81)§	0.68 (0.66-0.70)§
Proximal colon‖	13.1	21.3	25.4	0.62 (0.60-0.64)§	0.52 (0.50-0.54)§
Cecum (C18.0)	4.4	8.7	10.7	0.51 (0.48-0.55)§	0.41 (0.38-0.44)§
Ascending (C18.2)	3.8	6.2	7.0	0.61 (0.56-0.66)§	0.54 (0.49-0.60)§
Transverse plus two flexures (C18.3 to C18.5)	4.8	6.4	7.7	0.75 (0.70-0.80)§	0.62 (0.57-0.68)§
Distal colon	12.3	11.7	14.1	1.05 (1.00-1.10)	0.87 (0.82-0.92)§
Descending (C18.6)	1.9	1.9	3.0	1.00	0.63 (0.56-0.71)§
Sigmoid colon (C18.7)	10.4	9.7	11.1	1.07 (1.01-1.14)§	0.94 (0.88-1.00)
Rectum	10.5	11.9	11.5	0.88 (0.83-0.93)§	0.91 (0.85-0.97)§
Rectosigmoid junction (C19.9)	3.5	3.9	3.9	0.90 (0.81-1.00)	0.90 (0.80-1.01)
Rectum (C20.9)	7.1	7.9	7.7	0.90 (0.85-0.95)§	0.92 (0.85-0.99)§

*Rates are per 100,000 and age adjusted to the 2000 U.S. population standard.
†Source: NAACCR 1995 to 2000 analytic data file, including California, Colorado, Connecticut, Atlanta (Georgia), Hawaii, Iowa, Idaho, Illinois, Kentucky, Louisiana, Michigan, Minnesota, Nebraska, New Jersey, New Mexico, North Carolina, Pennsylvania, Rhode Island, Utah, Seattle/Puget Sound (Washington), West Virginia, Wisconsin, and Wyoming.
‡*International Classification of Diseases for Oncology, Second Edition* topograph codes are C18.0 to C18.9, C19.9, C20.9, and C26.0. Lymphomas were excluded.
§The rate ratio is significantly different ($P < 0.05$) from 1.00.
‖Appendiceal cancers were not included in this group.

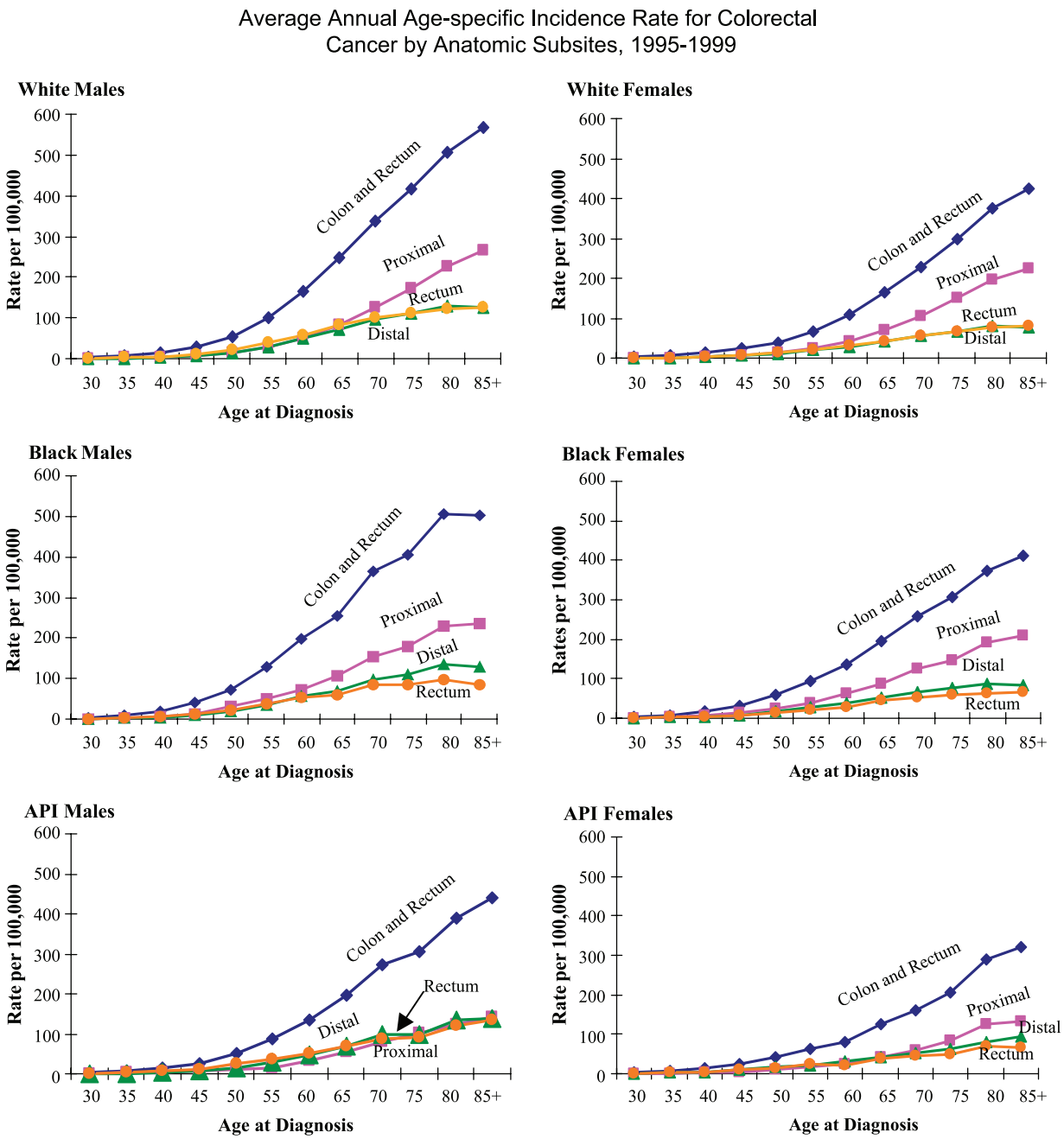

Figure 1. Average annual age-specific incidence rates per 100,000 for colorectal cancer by race, gender, and anatomic subsite, 1995 to 1999. Source: NAACCR 1995 to 2000 analytic data file, including California, Colorado, Connecticut, Atlanta (Georgia), Hawaii, Iowa, Idaho, Illinois, Kentucky, Louisiana, Michigan, Minnesota, Nebraska, New Jersey, New Mexico, North Carolina, Pennsylvania, Rhode Island, Utah, Seattle/Puget Sound (Washington), West Virginia, Wisconsin, and Wyoming.

For proximal and distal colon cancers, the percentages of localized stage were slightly higher among API than among African Americans for both males and females and about the same as among Whites. For rectal cancer, about half of the cases in API females were staged as localized, which was very high compared with White females (44%) and African American females (42%) while for males, the percentage of localized stage among API was slightly higher than among Whites and African Americans.

Discussion

Our study found that total colorectal cancer incidence rates in API were much lower than the rates in Whites and African Americans for both males and females; this finding is consistent with previous studies. Ries et al. (16) and Weir et al. (17) found that the 1990 to 2000 and 1996 to 2000 colorectal cancer incidence rates for API as a group were 13% lower than the rates for Whites and 25%

Table 3. Stage distributions of colorectal cancer by race and anatomic subsite for patients ≥50 years old, selected areas in the United States,* 1995 to 1999, males

Anatomic Subsite	API			Whites			Blacks		
	Localized	Regional	Distant	Localized	Regional	Distant	Localized	Regional	Distant
Colon and rectum†	40.5	42.5	17.1	38.7	42.7	18.6	34.7	40.7	24.6
Proximal‡	34.9	47.5	17.7	33.8	48.0	18.1	30.5	45.2	24.3
Cecum (C18.0)	33.6	47.2	19.2	31.0	47.6	21.4	29.5	43.6	26.9
Ascending (C18.2)	36.6	46.5	16.9	36.3	47.4	16.3	32.2	45.8	22.0
Transverse plus two flexures (C18.3 to C18.5)	34.7	48.3	16.9	33.1	50.4	16.4	30.1	46.5	23.4
Distal	41.4	41.6	17.0	42.2	39.6	18.2	38.8	38.8	22.4
Descending (C18.6)	37.3	45.6	17.1	38.5	45.1	16.4	38.9	40.0	21.2
Sigmoid colon (C18.7)	42.2	40.9	16.9	42.9	38.5	18.6	38.8	38.4	22.7
Rectum	44.8	39.9	15.3	42.3	40.6	17.1	39.5	37.0	23.5
Rectosigmoid junction (C19.9)	36.3	45.5	18.2	36.3	44.4	19.3	31.3	43.2	25.6
Rectum (C20.9)	48.9	37.2	13.8	45.3	38.7	16.0	43.6	33.9	22.5

*Source: NAACCR 1995 to 2000 analytic data file, including California, Colorado, Connecticut, Atlanta (Georgia), Hawaii, Iowa, Idaho, Illinois, Kentucky, Louisiana, Michigan, Minnesota, Nebraska, New Jersey, New Mexico, North Carolina, Pennsylvania, Rhode Island, Utah, Seattle/Puget Sound (Washington), West Virginia, Wisconsin, and Wyoming.
†*International Classification of Diseases for Oncology, Second Edition* topograph codes are C18.0 to C18.9, C19.9, C20.9, and C26.0. Lymphomas were excluded.
‡Appendiceal cancers were not included in this group.

lower than the rates for African Americans in the Surveillance, Epidemiology, and End Results areas. Using 1988 to 1992 Surveillance, Epidemiology, and End Results data, Miller et al. (18) also reported that incidence rates of colorectal cancer were lower for all API subgroups than for Whites and African Americans, except Japanese. The lower colorectal cancer incidence rates among API may reflect the influence of culture and socioeconomic differences in dietary habits, obesity, use of tobacco and/or alcohol, physical activity, and use of nonsteroidal anti-inflammatory drugs (19-24). Gene-environment interactions may also play a role (25, 26). Dietary factors are likely to have a major influence on risk of colorectal cancer. Migrant studies of dietary intake and dietary acculturation support the concept that, with a shift to a western diet after immigration, colorectal cancer incidence rates rise toward the risk levels of the new countries. However, the shift of diet and changes in the rates may take place over more than one generation (24, 27, 28). Because ~67% of API in the United States are first-generation immigrants who were born in Asia (29), traditional foods may still dominate the current dietary patterns among the API in the United States. However, consistent results have not been observed in the few dietary studies of ethnic minorities in the United States (30, 31). A dietary assessment study of Chinese Americans funded by the NIH found that total fat intakes and the distribution of fatty acid intake were not significantly different from other race groups (31). Nevertheless, both studies found that Chinese Americans and Native Hawaiians were more likely to have a plant-based diet, which was reflected by a higher contribution of carotene retinol equivalents and much higher vitamin C intake compared with Whites and African Americans. Because of the shortage of API dietary studies and the lack of consistency in study design and culturally sensitive

Table 4. Stage distributions of colorectal cancer by race and anatomic subsite for patients ≥50 years old, selected areas in the United States,* 1995 to 1999, females

Anatomic Subsite	API			Whites			Blacks		
	Localized	Regional	Distant	Localized	Regional	Distant	Localized	Regional	Distant
Colon and rectum†	39.9	43.0	17.2	37.1	45.0	17.9	33.5	43.3	23.2
Proximal‡	32.5	49.6	17.9	32.8	50.4	16.9	29.2	47.3	23.5
Cecum (C18.0)	32.1	48.3	19.6	32.1	48.6	19.3	28.9	44.6	26.5
Ascending (C18.2)	31.6	51.6	16.8	34.7	50.7	14.6	30.7	48.0	21.3
Transverse plus two flexures (C18.3 to C18.5)	33.5	49.2	17.2	31.7	52.5	15.7	28.3	50.5	21.3
Distal	38.8	43.1	18.1	39.9	41.9	18.2	36.5	42.7	20.9
Descending (C18.6)	32.7	55.1	12.2	36.6	46.9	16.5	34.4	48.0	17.6
Sigmoid colon (C18.7)	39.9	40.8	19.2	40.5	41.0	18.5	37.0	41.2	21.7
Rectum	51.1	35.0	13.8	44.4	39.5	16.2	42.2	37.7	20.1
Rectosigmoid junction (C19.9)	43.3	38.5	18.2	37.0	44.0	18.9	31.9	43.4	24.8
Rectum (C20.9)	55.1	33.3	11.6	48.2	37.1	14.7	47.9	34.5	17.5

*Source: NAACCR 1995 to 2000 analytic data file, including California, Colorado, Connecticut, Atlanta (Georgia), Hawaii, Iowa, Idaho, Illinois, Kentucky, Louisiana, Michigan, Minnesota, Nebraska, New Jersey, New Mexico, North Carolina, Pennsylvania, Rhode Island, Utah, Seattle/Puget Sound (Washington), West Virginia, Wisconsin, and Wyoming.
†*International Classification of Diseases for Oncology, Second Edition* topograph codes are C18.0 to C18.9, C19.9, C20.9, and C26.0. Lymphomas were excluded.
‡Appendiceal cancers were not included in this group.

dietary assessment methods, it is very difficult to draw a conclusion about overall diet quality and dietary patterns among API (32, 33). National data on diet and lifestyle among API are lacking in the United States. Previous National Health and Nutrition Examination Surveys collected race-specific data only for Whites and African Americans. All other races were combined as one group in the surveys. The National Health and Nutrition Examination Surveys IV (1999 to current) extends the race-specific categories to include all subgroups for API. Results from National Health and Nutrition Examination Surveys IV will give us better insight into the dietary and lifestyle differences between API and other races. Obesity increases the risk of colorectal cancer, especially among men (34). The 1992 to 1995 National Health Interview Survey found that the proportions of those who were overweight and obese were lower in the six largest Asian American groups (Chinese, Filipino, Asian Indian, Japanese, Korean, and Vietnamese) than in their White and African American counterparts for adults 18 to 59 years old (35). The same National Health Interview Survey data also showed that the proportion of overweight and obese increased with the increase in the proportion of U.S.-born Asian Americans and with duration of residence in the United States. Tobacco smoking is associated with elevated risk of colorectal cancer (36). Because the induction latency period of tobacco smoking probably spans several decades (34), recent data, which showed that Asian Americans had a lower percentage of current smokers than Whites and African Americans in the United States (37), may not help to explain the observed racial difference in the colorectal cancer incidence rate. Compared with other racial groups, API is the group least likely to report alcohol drinking, especially binge drinking (38). Physical activity has a significant inverse relationship with colorectal cancer (22, 39). According to the data from the 1997 Behavioral Risk Factor Surveillance System, the median percentage of persons who reported no leisure time physical activity is slightly higher among API (28.9%) than among Whites (25.1%) but lower than the percentages for other racial groups (38). Use of nonsteroidal anti-inflammatory drugs has also been associated with a reduced risk of colorectal cancer (40). However, data on use of nonsteroidal anti-inflammatory drugs among API in the United States are not available. Because colorectal cancer is a multifactorial disease, with complex interactions between genetic and environment factors, the reasons for lower colorectal cancer incidence rate among API than among Whites and African Americans are not well known.

Our data also showed that the rates of proximal colon cancer were markedly lower for API than for Whites and African Americans. Although numerous studies have been conducted to address colorectal cancer risk factors, most have combined colon and rectum as one group or have considered colon versus rectum. Very few epidemiologic studies have specifically examined risk factors for proximal colon cancer. Le Marchand et al. (41) conducted a case-control study among ethnic groups in Hawaii, including Japanese, White, Filipino, Hawaiian, and Chinese, to evaluate the effect of dietary lipids and foods of animal origin in the risk of colorectal cancer. They found that intake of red meat and processed meat was associated with the risk of proximal colon cancer in men only. Egg consumption has been associated with colon cancer, particularly for proximal colon cancer in females, suggesting a role for cholesterol in the etiology of proximal cancer (42). Cholecystectomy has also been associated with an elevated risk of proximal colon cancer (43, 44). Changes in the intestinal exposure to bile acids may be the primary biological mechanism (45). Certain bile acid metabolites selectively increase the risk of proximal colon cancer (46). Thomas et al. (3) and Weisburger et al. (47) speculated that the presence of high levels of secondary bile acids, derived from a high cholesterol diet, may serve to intensify the rate of cell cycling within the intestinal crypt and promote the development of cancer. However, associations of diet and lifestyle with risk of proximal colon cancer have not been consistently observed in epidemiologic studies. This phenomenon may be related to the influence of other concurrent risk factors. It has been reported that proximal colon cancer is more likely to be associated with genetic risk factors or uncharacterized carcinogens than distal colon and rectal cancers (48, 49). Further studies are needed to find explanations for the strikingly lower incidence rate of proximal colon cancer in API than in Whites and African Americans.

In the present study, although the rates of distal colon cancers were lower in API than in Whites and African Americans, the racial differences were much smaller than those for proximal colon cancer. For rectal cancer, the rate for API males was actually higher than the rate for African American males. Unlike proximal colon cancer, abundant epidemiologic studies have reported positive associations of high alcohol intake, tobacco smoking, red meat intake, and high serum albumin with increased risk of rectal cancer. These studies have also reported associations of a high intake of fruit, vegetable, and fiber; increased physical activity; higher percentage of carbohydrate calories; and high intake of dietary iron and calcium with reduction of risk of distal colon, especially rectal cancer risk (42, 50-54). Nonetheless, it is not well known how racial differences in these risk and protect factors contribute to the observed cancer incidence patterns of the distal colon and rectal cancers because race-specific information on these factors are scarce, especially for API. In addition, earlier studies suggest that variation in utilization of cancer screening by race and gender group may contribute to differences in observed incidence rates for the subsites that can be visualized and diagnosed earlier (55, 56). According to data from the 1997 Behavioral Risk Factor Surveillance System, percentage of API >50 years old who had sigmoidoscopy/proctoscopy during the preceding 5 years is lower than those of Whites and African Americans (37). However, it is not clear how the racial difference in colorectal cancer screening contributes to the racial difference in subsite-specific incidence rates of colorectal cancer. Because removing adenomatous polyps would reduce colorectal cancer incidence rates and screening may increase cancer incidence rates by detecting cancers years earlier than they would be diagnosed by symptoms, the effect of cancer screening on the colorectal cancer incidence rates is mixed. It is difficult to separate the effects of screening from actual racial and gender disparities in incidence rates, which may be associated with differences in exposure to subsite-specific risk factors.

Our data demonstrated that the rates of distal colon and rectal cancers were higher than proximal cancer for API males, while the opposite was found for Whites and African Americans. Reasons for the reverse pattern of subsite-specific rates in API males are unclear but may reflect different etiologies for cancers of the proximal colon, distal colon, and rectum. The proximal colon, distal colon, and rectum have different embryologic origins (48). Previous studies have found subsite variations in susceptibility to carcinogens and neoplastic transformation (57, 58). Molecular biological studies also indicate that tumor suppressor genes and point mutations and genetic instability differ by subsite of the colorectum (59-62).

Our study found that incidence rates increased with advancing age for all colorectal cancer subsites, but the increase was more pronounced for cancer occurring in the proximal colon than in the distal colon and rectum. Previous studies have noted this phenomenon (1, 2). This pattern was observed in all race and gender groups, except API males, for whom all three colorectal subsites (proximal colon, distal colon, and rectum) showed similar increases in incidence rates with advancing age. Neither the distinctive subsite-specific, age-specific incidence patterns for API males nor the intrinsic biological mechanisms of cancer growth at individual colorectal subsites with increasing age are well understood.

Our data also revealed that cancers in the proximal colon were less likely to be staged as localized disease at the time of diagnosis than cancers in the distal colon and rectum regardless of race and gender group. The subsite-specific stage distributions may reflect the impact of colorectal cancer screening. Because sigmoidoscopes cannot reach the proximal colon segment, and the annual fecal occult blood test is underused in the United States, cancers in the proximal colon are less likely than cancers in the distal colorectum to be detected early with the strategies applied for colorectal cancer screening during 1995 to 1999 (63-65). It has been reported that asymptomatic persons ≥50 years old who have polyps in the distal colon are more likely to have advanced proximal neoplasia than are persons without distal polyps (66, 67). However, if colonoscopic screening is performed only for persons with distal polyps, about half the cases of advanced proximal neoplasia will not be detected (68). It is not clear whether or how differences in tumor aggressiveness play a role in variations of tumor stage by anatomic subsite (48).

Two limitations of this study should be noted. First, racial misclassification is possible. Cancer incidence data used in this study were from population-based cancer registries. Although standard codes for race have been used in cancer registries in the United States, collection of race information has not been well standardized. Thus, some misclassification is expected in race information, although combining the API subgroups may reduce the possibility of misclassification for that race group as a whole. Second, because population data for subgroups of the API category were not available, this study had to analyze API as one group. ''API'' is a broadly inclusive category for a diverse group of cultures. The API population is not a homogenous group. The nativity ranges from <10% born in the United States, especially for Southeast Asian populations, to nearly 99% born in the United States for Native Hawaiians. These subpopulations may have different colorectal cancer risks due to distinct cultures, lifestyles, and diets and may obscure real differences among race groups. For instance, although overall API rates are lower than the rates for Whites and African Americans in the United States, several studies have reported that the incidence of colorectal cancer among Japanese who immigrated to the United States increased quickly and matched that of Whites as early as the first generation (18, 25, 26).

Population-based cancer registry programs (the Surveillance, Epidemiology, and End Results Program sponsored by the National Cancer Institute and the National Program of Cancer Registries sponsored by the Centers for Disease Control and Prevention) in the United States endow us with very good cancer surveillance data. However, findings based on the surveillance data should serve as a foundation to guide the direction of cancer research. With regard to subsite-specific colorectal cancer risk factors and racial differences, several outstanding issues remain unexplained. Because colorectal cancer is one of the most common cancers, it is important to conduct further studies to address these issues. Racial diversity in the population and the high percentage of immigrants in the United States provide us with a unique opportunity to study the etiology of colorectal cancer. More research regarding minority health behavior, which has been consistently unrepresented, is also very much needed.

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