Proximal Tumors Are Associated with Greater Mortality in Colon Cancer

Robert Wong, MD

Department of Medicine, California Pacific Medical Center, San Francisco, CA, USA.

BACKGROUND: Colon cancer is the third leading cause of death from cancer in the United States. Recent studies report on increasing proportions of proximal cancers. The etiology behind this epidemiological trend is unclear, and its implication on survival outcomes is unknown. Further analysis of the impact of anatomic site of disease among a large multiethnic population will help facilitate research and education to improve colon cancer screening and treatment.

OBJECTIVE: To investigate the association between proximal tumor location and survival in patients with colon cancer.

DESIGN AND PARTICIPANTS: A large retrospective cohort study in the US utilizing the Surveillance, Epidemiology, and End Results (SEER) cancer registry analyzed survival outcomes of patients with colon cancer. Multivariable logistic regression analyses investigated sex-specific, race/ethnicity-specific, and anatomic site-specific disparities in survival.

MAIN MEASURES: Five-year survival outcomes from colon cancer.

RESULTS: Our study demonstrated significant disparities in survival by sex, race/ethnicity, and anatomic site. Across all time periods and among most cohorts, patients with proximal cancers had significantly worse survival outcomes. When compared to distal cancers, patients with proximal cancers were 13% less likely to survive 5 years (OR 0.87; 95% CI, 0.82–0.91). When compared to non-Hispanic whites, blacks were 30% less likely to survive 5 years (OR 0.70; 95% CI, 0.68–0.73). Stage-specific multivariable regression analysis of localized cancers demonstrated similar findings.

CONCLUSIONS: Significant race-specific, sex-specific, and anatomic site-specific disparities in colon cancer survival exist. Proximal cancers are associated with worse survival odds. These disparities may reflect differences in the genotype and phenotype of colon cancer among these groups. A modified risk assessment tool that incorporates these variations may be more effective in the early detection and treatment of colon cancer.

KEY WORDS: colorectal cancer; cancer screening; epidemiology.

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INTRODUCTION

Colon cancer is the third leading cause of death from cancer in the US among men and women.¹ The institution of widespread screening and surveillance programs for early detection and treatment of colon cancer has led to significant improvements in mortality.^{2–4} However, recent studies have reported on sex-specific and race/ethnicity-specific disparities that persist despite the overall improvements achieved. For example, males and blacks demonstrated consistently worse colon cancer survival outcomes when compared to females and non-Hispanic whites, respectively.^{5–11} Whether these differences result from inherent variations in group-specific cancer biology or reflect variations in health care access that may affect timely detection and treatment is unclear.

Recent studies have also reported on the changing epidemiology of colon cancer with an increasing trend towards more right-sided or proximally located disease.^{11–17} These trends may not necessarily reflect a net increase in the incidence of proximal colon cancers, but rather a more significant decline in distal or left-sided cancers, thereby affecting the overall proportional distribution of disease by anatomic site. Blacks and females are disproportionately affected by this shift as these groups demonstrated greater degrees of proximally distributed disease.^{11–13} Survival benefits from current cancer screening programs have been called into question for proximal disease, and some have suggested that differences in epidemiology may necessitate more frequent screening intervals among this cohort.^{14–18} The impact of this shifting distribution towards more proximal disease and whether the anatomic site of colon cancer at diagnosis predicts survival outcomes are unclear. Knowledge of anatomic site-specific survival outcomes among a large representative cohort will be important in guiding research and education to evaluate current colon cancer screening programs. In the current study, we aimed to further delineate the epidemiology of proximal and distal colon cancers, survival disparities among a large multiethnic population, and whether the proximal location of cancer is associated with worse survival outcomes.

METHODS

Data Sources

The Surveillance, Epidemiology, and End Results (SEER) database is a comprehensive population-based registry that collects information on cancer prevalence, incidence, and survival in the US. The 1973–2005 dataset includes cancer

data for expanded race/ethnicity classifications and incorporates data from 13 states: Alaska, California, Connecticut, Georgia, Hawaii, Iowa, Kentucky, Louisiana, Michigan, New Jersey, New Mexico, Utah, and Washington.^{19,20}

Case Definitions

Cases of colon cancer were identified using the International Classification of Disease for Oncology, 3rd edition.²¹ Detailed information on stage of disease and tumor localization was available. Cancer localization was based on the SEER system of recording anatomic site of disease: proximal colon (cecum, appendix, ascending colon, and hepatic flexure), transverse colon, and distal colon (splenic flexure, descending colon, sigmoid colon, rectosigmoid junction, and rectum). Subset analyses that excluded rectal cancers were also included. Cancer stages were based on SEER staging systems: “localized” cancers are confined to the colon without transmural invasion to or beyond the serosa; “regional” cancers have spread beyond the serosa or have evidence of regional lymph node involvement; “advanced” cancers have evidence of distant lymph node involvement or metastatic disease.²²

Age-Specific and Year-Specific Analyses

Age of cancer diagnosis and year of cancer diagnosis were included in our evaluation. In addition to inclusion of age as a continuous variable in multivariable logistic regression analyses, we also evaluated survival outcomes using age cohorts (<40 years old, 40–60 years old, >60 years old). The same methodology was applied to data for year of cancer diagnosis. The current study utilized two different time periods for analysis (1983–1997 and 1998–2005). The rationale for utilizing this type of categorization reflects the way SEER compiles its cancer treatment data. From 1983–1997 and 1998–2005, SEER utilized two different methods for categorizing treatment data. In both time periods, SEER records the first treatment regimen, and not necessarily the most recent or most definitive form of therapy received. The current study included treatment data in multivariable regression analyses, and for consistency of comparisons, similar time periods were studied. Prior to 1983, the treatment data available were less clear and less consistent for analysis.

Outcome Definitions

The main outcome was the proportion of patients surviving 5 years after diagnosis of colon cancer. The study evaluated the association between tumor anatomy and 5-year survival after a diagnosis of colon cancer using multivariable logistic regression models.

Statistical Analysis

Analyses were performed using the SEER*Stat 6.5.3 (National Cancer Institute, MD) and the Stata statistical packages (release ten, Stata Corporation, TX). SEER Stat is a publicly

available statistical software program for the analysis of SEER and cancer databases. In addition to calculation of cancer frequency and prevalence, age-adjusted analyses of cancer incidence and survival are available. Multivariable logistic regression models were adjusted for sex, age, year of diagnosis, race/ethnicity, cancer stage, anatomic site of disease, geography, and treatment received. These criteria were selected based on their inclusion in prior studies to ensure consistency of comparisons and analyses. Odds ratios (OR) and 95% confidence intervals (CI) were calculated using regression models with an outcome measure of 5-year survival. P-values for comparisons were calculated using standard equations.²³

RESULTS

Overview

The mean proportion of patients surviving 5 years after a diagnosis of colon cancer from 1973–1997 was 45.1% (44.7–45.5) in females and 42.8% (42.4–43.2) in males. During the same time period, blacks had the worst 5-year survival (39.2%; 95% CI, 38.2–40.4) and Asians had the best 5-year survival (51.5%; 95% CI, 50.4–52.4) (Table 1). Across all time periods and among most cohorts, 5-year survival among patients with proximal tumors was generally lower when compared with distal tumors (Table 1).

Trends in 5-Year Survival Outcome

Table 1 presents detailed 5-year survival data stratified by sex, race/ethnicity, and anatomic site of disease. Among all time periods and for most cohorts, patients with proximal cancers had poorer survival when compared to patients with distal cancers. For example, from 1973–1997, males with proximal cancers had lower 5-year survival than males with distal cancers (41.3% vs. 43.4%, $p < 0.001$). Similar findings persisted for the more recent time period (1998–2005, males, 5-year survival; proximal: 44.5% vs. distal: 49.4%, $p < 0.001$).

Improvements in 5-year survival from 1973–1997 and 1998–2005 were seen for all stages of disease (Table 1 and Figure 1). Even among advanced stage disease, where the overall 5-year survival is less than 8%, a small, statistically significant improvement was demonstrated. For example, 5-year survival for advanced stage proximal cancers improved from 5.8% (95% CI, 5.5–6.1) in 1973–1997 to 7.5% (95% CI, 6.4–8.6) in 1998–2005, $p < 0.01$. Improved survival outcomes across time periods were similar among all cohorts and did not differ between proximal disease and distal disease (Table 1).

Adjusted Site-Specific Survival Analysis

Multivariable logistic regression analyses were performed for 5-year survival outcomes. Table 2 presents the regression analysis from 1973–2005. Patients with proximally located

Table 1. Five-Year Survival in Patients Diagnosed with Colon Cancer, Stratified by Sex, Race/Ethnicity, Stage of Disease, and Anatomic Site

	Proximal site		P-values	Distal site		P-values	P-values total
	Percent (%)	95% CI	Site specific	Percent (%)	95% CI	Site specific	
1973–1997							
Sex							
Female	44.1%	(43.7–44.5)	Reference	45.6%	(45.3–45.9)	Reference	0.001
Male	41.3%	(40.8–41.8)	<0.001	43.4%	(43.1–43.7)	<0.001	<0.001
Race/ethnicity							
Non-Hispanic white	42.7%	(42.4–43.0)	Reference	44.3%	(44.1–44.5)	Reference	<0.001
Black	39.3%	(38.2–40.4)	<0.001	39.2%	(38.4–40.0)	<0.001	0.88
Asian	49.8%	(48.2–51.4)	<0.001	51.9%	(51.0–52.8)	<0.001	0.02
Hispanic	46.7%	(44.9–48.5)	<0.001	45.2%	(44.1–46.3)	0.11	0.16
Stage of disease							
Localized	64.8%	(64.3–65.3)	Reference	67.4%	(67.1–67.7)	Reference	<0.001
Regional	47.1%	(46.6–47.6)	<0.001	45.7%	(45.3–46.1)	<0.001	<0.001
Advanced	5.8%	(5.5–6.1)	<0.001	5.4%	(5.2–5.6)	<0.001	0.02
1998–2005							
Sex							
Female	47.6%	(46.4–48.8)	Reference	50.3%	(49.3–51.3)	Reference	<0.001
Male	44.5%	(43.2–45.8)	<0.001	49.4%	(48.5–50.3)	0.19	<0.001
Race/ethnicity							
Non-Hispanic white	46.3%	(45.3–47.3)	Reference	44.9%	(44.2–45.6)	Reference	0.02
Black	41.8%	(39.1–44.5)	<0.01	42.1%	(40.0–44.2)	0.01	0.86
Asian	52.4%	(48.8–56.0)	<0.01	55.6%	(53.5–57.7)	<0.001	0.13
Hispanic	46.6%	(43.0–50.2)	0.87	50.0%	(47.6–52.4)	<0.001	0.12
Stage of disease							
Localized	65.1%	(63.8–66.4)	Reference	70.3%	(69.4–71.2)	Reference	<0.001
Regional	49.8%	(48.5–51.3)	<0.001	53.3%	(52.2–54.4)	<0.001	<0.001
Advanced	7.5%	(6.4–8.6)	<0.001	7.3%	(6.5–8.1)	<0.001	0.77

*SEER dataset time periods 1973–1997 and 1998–2005

P-value site specific analyses compare values vertically down the table within each group. For example, within the 1973–1997 cohort, survival for proximal tumors for different races are compared to the survival among non-Hispanic whites as the references group. P-values total compares survival between proximal tumors and distal tumors across the table. For example, within the 1973–1997 cohort, cancer survival among females with proximal tumors is compared to females with distal tumors

Figure 1. Trends in 5-year survival from colon cancer stratified by stage of disease and anatomic site. Legend designations indicate the anatomic site and stage of disease. For example, "proximal-local" refers to patients with localized disease in the proximal colon.

Table 2. Multivariable Logistic Regression Analysis of 5-Year Survival from Colon Cancer, 1973–2005

Predictor variable	Adjusted OR	95% CI
Sex		
Female	Reference	-
Male	0.80	(0.79–0.81)
Age		
<40 years	Reference	-
40–60 years	0.94	(0.88–0.99)
>60 years	0.48	(0.46–0.51)
Race/ethnicity		
Non-Hispanic white	Reference	-
Black	0.79	(0.76–0.81)
Asian	1.21	(1.17–1.24)
Hispanic	0.95	(0.91–0.98)
Stage of disease		
Localized	Reference	-
Regional	0.43	(0.41–0.43)
Advanced	0.03	(0.02–0.03)
Anatomic site		
Distal colon	Reference	-
Proximal colon	0.91	(0.89–0.92)
Anatomic site (excluding rectal cancers)		
Distal colon	Reference	-
Proximal colon	0.89	(0.88–0.91)

*The odds ratio is adjusted for sex, age of diagnosis, race/ethnicity, stage of disease, anatomic site of disease, and geographic region. Additional analysis of anatomic site after exclusion of rectal cancers is included.

cancers were about 10% less likely to survive 5 years (OR 0.91; 95% CI, 0.89–0.92). After excluding rectal cancers from the analysis, this difference persisted (proximal colon cancer, 5-year survival: OR 0.89; 95% CI, 0.88–0.91) (Table 2). In an attempt to further delineate the etiology of this variation, we investigated whether treatment variations between proximal and distal cancers could affect survival outcomes. In addition, we investigated whether advances in treatment approach across time periods may also have contributed to these findings. Table 3 presents a survival regression analysis that includes treatment data. As described above, the SEER dataset utilized two different categories to document cancer therapy from 1983–1997 and 1998–2005. Our analysis used these two time periods for consistency of comparisons. For both time periods, patients with proximal cancers consistently demonstrated worse survival odds. For example, from 1983–1997, patients with proximal cancers were nearly 10% less likely to survive 5 years (OR 0.91; 95% CI, 0.84–0.98), and from 1998–2005 patients with proximal cancers were 6% less likely to survive 5 years (OR 0.94, 95% CI, 0.92–0.96) (Table 3). After excluding rectal cancers, site-specific variations in cancer mortality persisted with greater statistical significance (proximal cancer, 5-year survival, 1983–1997: OR 0.88; 95% CI, 0.86–0.90; 1998–2005: OR 0.87; 95% CI, 0.82–0.91).

Adjusted Site-Specific Survival Analysis Among Localized Tumors

Compared to advanced stage disease, localized cancers have significantly better outcomes with overall 5-year survival ranging from 64–70% (Table 1). The diagnostic and treatment

approaches to localized tumors are generally more uniform and have more consistent prognoses. Inter-stage variability in diagnostic staging and treatment is believed to be less significant than more advanced stages of disease. A detailed analysis that focuses on localized disease may more accurately demonstrate survival benefits from interventions and improve the ability to identify the impact of independent factors on overall survival. Table 4 presents a multivariable logistic regression analysis of 5-year survival among patients with localized colon cancer. Initial analyses of site-specific variations in survival demonstrated weak associations. Among both time periods, proximal cancers demonstrated a trend towards greater 5-year mortality, but these differences did not reach statistical significance. After excluding rectal cancers, site-specific survival differences were greater in magnitude and statistical significance. For example, patients with proximal colon cancer from 1983–1997 were 16% less likely to survive 5 years compared to distal cancers (OR 0.84; 95% CI, 0.81–0.86) (Table 4).

Demographic Variations in Survival

For all time periods and for both proximal cancers and distal cancers, males and blacks as a group had worse overall 5-year survival (Table 1). Similar trends were demonstrated in multivariable logistic regression models (Tables 2 and 3). Inclusion of treatment data in the regression model did not mitigate these disparities. For example, compared to non-Hispanic whites, blacks with colon cancer during the 1983–1997 period were 34% less likely to survive 5 years (OR 0.66; 95% CI, 0.58–0.73), and males during the 1998–2005 period were 18% less

Table 3. Multivariable Logistic Regression Analysis of 5-Year Survival with Inclusion of Treatment Data

Predictor variable	1983–1997	95% CI	1998–2005	95% CI
	Adjusted OR		Adjusted OR	
Sex				
Female	Reference	-	Reference	-
Male	0.85	(0.80–0.92)	0.82	(0.80–0.84)
Age				
<40 years	Reference	-	Reference	-
40–60 years	0.88	(0.69–1.12)	0.96	(0.89–1.03)
>60 years	0.42	(0.33–0.53)	0.50	(0.47–0.54)
Race/ethnicity				
Non-Hispanic white	Reference	-	Reference	-
Black	0.66	(0.58–0.73)	0.70	(0.68–0.73)
Asian	1.04	(0.92–1.17)	1.14	(1.10–1.19)
Hispanic	0.78	(0.68–0.89)	0.86	(0.82–0.90)
Stage of disease				
Localized	Reference	-	Reference	-
Regional	0.44	(0.41–0.47)	0.39	(0.38–0.40)
Advanced	0.02	(0.01–0.02)	0.02	(0.02–0.02)
Anatomic site				
Distal colon	Reference	-	Reference	-
Proximal colon	0.91	(0.84–0.98)	0.94	(0.92–0.96)
Anatomic site (excluding rectal cancers)				
Distal colon	Reference	-	Reference	-
Proximal colon	0.88	(0.86–0.90)	0.87	(0.82–0.91)

*The above analyses adjusted for age, sex, race/ethnicity, stage of disease, anatomic site of disease, geographic region, and treatment. Two different categories of cancer therapy were used in the SEER dataset from 1983–1997 and 1998–2005. The above analyses separate these time periods for consistency of comparisons

Additional analysis of anatomic site after exclusion of rectal cancers is included

Table 4. Multivariable Logistic Regression Analysis of 5-Year Survival from Localized Colon Cancer

Predictor variable	1983–1997	95% CI	1998–2005	95% CI
	Adjusted OR		Adjusted OR	
Sex				
Female	Reference	-	Reference	-
Male	0.71	(0.69–0.74)	0.78	(0.70–0.87)
Age				
<40 years	Reference	-	Reference	-
40–60 years	0.81	(0.68–0.97)	1.02	(0.61–1.70)
>60 years	0.25	(0.21–0.29)	0.27	(0.16–0.44)
Race/ethnicity				
Non-Hispanic white	Reference	-	Reference	-
Black	0.64	(0.61–0.68)	0.68	(0.56–0.82)
Asian	1.22	(1.14–1.30)	1.09	(0.90v1.33)
Hispanic	0.81	(0.75–0.88)	0.87	(0.68–1.11)
Anatomic site				
Distal colon	Reference	-	Reference	-
Proximal colon	0.97	(0.94–1.00)	0.89	(0.79–1.01)
Anatomic site (excluding rectal cancers)				
Distal colon	Reference	-	Reference	-
Proximal colon	0.84	(0.81–0.86)	0.85	(0.78–0.92)

*The above analysis is adjusted for sex, age, race/ethnicity, anatomic site, geography, and treatment

Two different categories of cancer therapy were used in the SEER dataset from 1983–1997 and from 1998–2005. The above analyses separate these time periods for consistency of comparisons

Additional analysis of anatomic site after exclusion of rectal cancers is included

likely to survive 5 years compared to females (OR 0.82; 95% CI, 0.80–0.84) (Table 3). Similar trends persisted when focusing the analysis on localized cancers (Table 4).

DISCUSSION

Our large population-based study demonstrated significant anatomic site-specific disparities in colon cancer survival in the US. Patients with proximal colon cancers had significantly worse 5-year survival when compared to patients with distal cancers. This survival difference persisted among most groups and across most time periods. Even after adjusting for potential confounding factors including stage of disease at diagnosis and treatment received, proximal cancers were 13% less likely to survive 5 years when compared to distal cancers (Table 3). While the etiology behind these site-specific differences is unclear, variations in tumor biology, screening practices, and inter-stage variability may play a role. Some studies have suggested higher miss rates on colonoscopy for proximal cancers due to variations in technique and skill, resulting in more advanced disease at presentation.^{12,13,17} Proximal lesions tend to be smaller in size and more often non-polypoid flat in appearance, further contributing to greater miss rates on colonoscopy. This phenomenon would lead to disparities in stage of disease between proximal and distal cancers with more advanced stages of disease at presentation accounting for the relatively greater mortality among proximal disease. Even after adjusting for stage of disease at presentation, our regression analysis continued to demonstrate anatomic site-specific survival disparities. For similar staged disease, it is unlikely that significant treatment variations exist between proximal and distal cancers. Nevertheless, our regression analysis also adjusted for therapy received. The significantly greater mortality among proximal cancers persisted.

Inter-stage variability and a component of Will Rogers bias may partially account for survival differences. As stated in our methods, SEER utilizes a relatively simple staging system primarily for categorization of disease and not necessarily for prognostic determination. A spectrum of disease exists within each category such that “regional” cancers from two separate cohorts may have varying degrees of disease progression and mortality. Furthermore, the Will Rogers bias, which suggests that “localized” cancers from one time period may be more accurately classified as “regional” or “advanced” in a different time period, could lead to inaccurate survival data. Our study performed a detailed stage-specific analysis that focused on localized tumors. While Will Rogers bias and inter-stage variability may still occur, their impact on this subset analysis is expected to be less significant because all patients are subject to the same biases. In our study, stage-specific analysis of localized cancers continued to demonstrate site-specific variations: patients with proximal cancers were 15% less likely to survive 5 years compared to those with distal cancers.

Variations in tumor biology have been implicated in cancer incidence and survival disparities. Studies have suggested that disease biology is different between proximal colon cancers and distal colon cancers.^{24–28} For example, microsatellite instability and CpG island methylation are more common in proximal cancers, whereas chromosomal instability is more characteristic of distal cancers.²⁵ These molecular distinctions are important in light of recent evidence demonstrating variations in response to adjuvant chemotherapy based on specific microsatellite instability markers.^{29,30} It is conceivable that inherent differences in colon cancer biology not only affect disease progression, but also response to therapy and prognosis. The idea that certain cohorts have variations in response to treatment that affect health outcomes is not novel. For example, prior studies have reported on race-/ethnicity-specific responses to treatment for diseases such as hepatitis C,³¹ hypertension,^{32–34} and hepatocellular

carcinoma.³⁵ These differences likely reflect variations in genetic predisposition (e.g., disease genotype) and unmeasured risk factors, but there is an implication that for similarly staged disease, race or anatomic site of disease may be an independent factor that predicts prognosis. Modifying colon cancer screening and surveillance programs to incorporate these findings may take place in the near future as more studies begin to investigate clinical implications of the disparate epidemiology of proximal colon cancers.

Prior studies have demonstrated significant race-specific and sex-specific disparities in colon cancer survival.^{5–11,36} In our study, blacks and males demonstrated the worst survival outcomes among all stages of disease and among both proximal and distal cancers (Table 1). These sex-specific and race-specific disparities persisted after adjusting for multiple factors including geography, stage of disease, and treatment received (Tables 2, 3 and 4). While disparities in cancer screening and treatment may underlie some of these findings, continued evidence of sex-specific and race-specific survival differences after adjusting for treatment and stage of disease suggests that issues of access to health care or tumor biology may be more significant factors. Patients with sub-optimal health care access (e.g., timely cancer screening and detection) may have more advanced disease at presentation, less options for curative therapy, and greater mortality. While differences in cancer biology have been implicated for anatomic site-specific survival, no studies have demonstrated clear evidence to suggest race-/ethnicity-specific variations in colon cancer pathogenesis.

Strengths of this study include the utilization of high quality data from a large population-based cancer registry that represents a large proportion of the US population. Detailed data on race classifications and therapeutic interventions permitted in-depth survival analyses using multivariable logistic regression models. The ability to stratify and incorporate stage of disease and anatomic site of disease facilitated an accurate evaluation of their impact on overall survival.

Potential limitations include the categorization scheme utilized by the SEER database for cancer stage. The SEER staging system is unique to the SEER database and is used primarily for classification of disease, not necessarily for prognostic determination. Furthermore, within each category of cancer stage, a spectrum of disease can exist. For example, while “localized” cancers are defined as being confined to the colon without transmural invasion to or beyond the serosa, it does not discern into greater detail the depth of tumor invasion or take into account the number of tumors present. These additional tumor characteristics may affect accurate classification. For example, both American Joint Committee on Cancer (AJCC) stage I and stage IIA tumors would be included as “localized” in the SEER database. Our survival analysis adjusted for stage of disease in regression models, and variations in spectrum of disease within each cancer stage would not fully account for the significant disparities seen. The retrospective nature of our study also limited the inclusion of important risk factors (e.g., family history of cancer, comorbidities, tobacco and alcohol use, diet) that would impact disease progression, treatment options, and overall survival. Furthermore, stage-specific survival analysis of localized tumors may have been confounded by lead-time bias.

In summary, our study demonstrates significantly lower 5-year survival for patients with proximal colon cancer compared

to distal colon cancer. These variations may reflect the distinct genotype and phenotype of proximal colon cancers and may imply a need for a modified approach to these tumors.^{24–28} Variations in race-/ethnicity-specific and sex-specific survival outcomes may also reflect different genetic predisposition, disease biology, or disparities in access to health care. Incorporating these concepts into research and education will be paramount to the future role of genetics in disease prevention and management. A modified risk assessment tool that incorporates colon cancer disparities may be more effective in early detection and treatment.

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Corresponding Author: Robert Wong, MD; Department of Medicine, California Pacific Medical Center, 2351 Clay Street, Suite 380, San Francisco, CA 94115, USA (e-mail: RobertWong123@gmail.com).

REFERENCES

1. American Cancer Society. Cancer Facts and Figures 2009. Atlanta: American Cancer Soc; 2009. Accessed at <http://www.cancer.org/Research/CancerFactsFigures/index> on July 3, 2010.
2. Levin B, Lieberman DA, McFarland B, Smith RA, Brooks D, Andrews KS, et al. American Cancer Society Colorectal Cancer Advisory Group. Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps, 2008: a joint guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. *CA Cancer J Clin.* 2008;58: 130–60.
3. Cooper GS, Yuan Z, Landefeld S, et al. A national population based study of incidence of colorectal cancer and age. *Cancer.* 1995;75:775–81.
4. Winawer SJ, Zauber AG, Ho MN, et al. Prevention of colorectal cancer by colonoscopic polypectomy. *New Engl J Med.* 1993;329:1977–81.
5. Singh SM, Paszat LF, Li C, He J, Vinden C, Rabeneck L. Association of socioeconomic status and receipt of colorectal cancer investigations: a population-based retrospective cohort study. *CMAJ.* 2004;171:461–5.
6. Ward E, Jemal A, Cokkinides V, et al. Cancer disparities by race/ethnicity and socioeconomic status. *CA Cancer J Clin.* 2004;54:78–93.
7. Agrawal S, Bhupinderjit A, Bhutani M, et al. Colorectal cancer in African Americans. *Am J Gastroenterol.* 2005;100:515–23.
8. Chu KC, Miller B, Springfield S. Measures of racial/ethnic health disparities in cancer mortality rates and the influence of socioeconomic status. *J Natl Med Assoc.* 2007;99:1092–1104.
9. Irby K, Anderson W, Henson D, et al. Emerging and widening colorectal carcinoma disparities between blacks and whites in the United States (1975–2002). *Cancer Epidemiol Biomarkers Prev.* 2006;15:792–97.
10. Carethers JM. Race and ethnic factors in the genetic pathogenesis of colorectal cancer. *J Assoc Acad Minor Phys.* 1999;10:59–67.
11. Wong RJ. Marked variations in colon cancer epidemiology: sex-specific and race/ethnicity-specific disparities. *Gastroenterol Res.* 2009;5:268–76.
12. Rabeneck L, Davila JA, El-Serag HB. Is there a true “shift” to the right colon in the incidence of colorectal cancer? *Am J Gastroenterol.* 2003;98:1400–09.
13. Cucino C, Buchner AM, Sonnenberg A. Continued rightward shift of colorectal cancer. *Dis Colon Rectum.* 2002;45:1035–40.
14. Rabeneck L, Lewis JD, Paszat LF, Saskin R, Stukel TA. Risk of proximal and distal colorectal cancer following flexible sigmoidoscopy: a population-based cohort study. *Am J Gastroenterol.* 2008;103:2075–82.
15. Lakoff J, Paszat LF, Saskin R, Rabeneck L. Risk of developing proximal versus distal colorectal cancer after a negative colonoscopy: a population-based study. *Clin Gastroenterol Hepatol.* 2008;6:1117–21.
16. Baxter NN, Goldwasser MA, Paszat LF, et al. Association of colonoscopy and death from colorectal cancer. *Ann Intern Med.* 2009;150:1–8.
17. Bressler B, Paszat LF, Vinden C, Li C, He J, Rabeneck L. Colonoscopic miss rates for right-sided colon cancer: a population-based analysis. *Gastroenterology.* 2004;127:452–6.

18. **Ransohoff DF.** Five-year risk of colorectal neoplasia after negative screening colonoscopy. *N Engl J Med.* 2008;359:1218–24.
19. **Ries LAG, Melbert D, Krapcho M, et al., eds.** SEER cancer statistics review, 1975–2005. Bethesda, MD: National Cancer Institute; 2008.
20. Surveillance, Epidemiology, and End Results (SEER) Program Public Use CD-ROM. (1973–2005). National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2008.
21. World Health Organization. International Classification of Diseases for Oncology. 3rd ed. Geneva, Switzerland: World Health Organization; 2000.
22. **Young JL, Roffers SD, Ries LAG, et al., eds.** SEER Summary Staging Manual–2000: Codes and Coding Instructions. Bethesda, MD: National Cancer Institute; 2001.
23. **Silva IS.** Cancer Epidemiology: Principles and Methods. Geneva, Switzerland: World Health Organization; 2001.
24. **Gervaz P, Bucher P, Morel P.** Two colons—two cancers: paradigm shift and clinical implications. *J Surg Oncol.* 2004;88:261–266.
25. **Chirieac LR, Shen L, Catalano PJ, et al.** Phenotype of microsatellite-stable colorectal carcinomas with CpG island methylation. *Am J Surg Pathol.* 2005;29:429–436.
26. **Konishi K, Fujii T, Boku N, et al.** Clinicopathological differences between colonic and rectal carcinomas: are they based on the same mechanism of carcinogenesis? *Gut.* 1999;45:818–821.
27. **Hurlstone DP, Cross SS, Adam I, et al.** A prospective clinicopathological and endoscopic evaluation of flat and depressed colorectal lesions in the United Kingdom. *Am J Gastroenterol.* 2003;98:2543–2549.
28. **Ross AS, Waxman I.** Flat and depressed neoplasms of the colon in western populations. *Am J Gastroenterol.* 2006;101:172–180.
29. **Boland CR, Goel A.** Microsatellite instability in colorectal cancer. *Gastroenterol.* 2010;138:2073–2087.
30. **Sargent DJ, Marsoni S, Monges G, Thibodeau SN, Labranci R, Hamilton SR.** Defective mismatch repair as a predictive marker for lack of efficacy of Fluorouracil-based adjuvant therapy in colon cancer. *J Clin Oncol.* 2010 [E-pub ahead of print] PMID:20498393.
31. **Mchutchinson L, Poynard T, Pianko S, et al.** The impact of interferon plus ribivirin on response to therapy in blacks with chronic hepatitis C. *Gastroenterology.* 2000;119:1317–23.
32. **Park IU, Taylor AL.** Race and ethnicity in trials of antihypertensive therapy to prevent cardiovascular outcomes: a systematic review. *Ann Fam Med.* 2007;5:444–52.
33. The ALLHAT Officers Coordinators for the ALLHAT Collaborative Research Group. Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker versus diuretic: the antihypertensive and lipid-lowering treatment to prevent heart attack trial (ALLHAT). *JAMA.* 2002;288:2891–97.
34. **Gibbs CR, Beevers DG, Lip GY.** The management of hypertensive disease in black patients. *Q J Med.* 1999;92:187–92.
35. **Wong RJ, Corley DA.** Survival differences by race/ethnicity and treatment for localized hepatocellular carcinoma within the United States. *Dig Dis Sci.* 2009;54:2031–2039.
36. **Wong RJ.** Marked Variations in Proximal Colon Cancer Survival by Race/Ethnicity Within the United States. *J Clin Gastroenterol.* 2009 [Epub ahead of print] PMID: 19996985