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Racial/ethnic disparities in the adjuvant chemotherapy of locally advanced colon cancer patients

Xi Zhong, MD,[1] *Zhexu Guo, MD,*[1] *Peng Gao, MD, Yongxi Song, MD, PhD, Jingxu Sun, MD, Xiaowan Chen, MD, Yu Sun, MD, and Zhenning Wang, MD, PhD*[*]

Department of Surgical Oncology and General Surgery, The First Hospital of China Medical University, Shenyang City, PR China

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ABSTRACT

Background: Most race/ethnicity-oriented investigations focus on Caucasian Americans (whites) and African Americans (blacks), leaving Asians, Hispanic white (Hispanics), and other minorities less well studied. Adjuvant chemotherapy (CT) after curative resection is critical to patients with locally advanced colon cancer (LACC). We studied the racial disparities in the adjuvant CT of LACC to aid in selecting optimal treatments for people from different races/ethnicities in this era of precision medicine.

Methods: Patients with American Joint Committee on Cancer (AJCC) stage II or III colon cancer (CC) (together termed as LACC) were included based on Surveillance, Epidemiology, and End Results cancer registry–Medicare linked databases. The log-rank test and Cox multivariate regression analysis were performed to investigate the racial/ethnic disparities in cohorts divided according to the regimen of adjuvant CT.

Results: In the LACC patients who did not receive adjuvant CT, Asian patients had better survival than other groups (all, $P < 0.05$). For the fluoropyrimidine cohort, the survival of Asian patients was better than that of whites, blacks, and other minorities (all, $P < 0.05$). For the fluoropyrimidine with oxaliplatin cohort, other minorities had superior survival to other groups (all, $P < 0.05$). Similar findings were demonstrated for patients with AJCC stage II and III CC, and the observed better survival persisted after adjustments in the Cox models.

Conclusions: Among LACC patients not receiving adjuvant CT, Asians achieved better survival than other races/ethnicities. Superior survival was also observed for Asians in the fluoropyrimidine cohort and for other minorities in the fluoropyrimidine with oxaliplatin cohort for AJCC stage III CC.

Introduction

Colorectal cancer is one of the most lethal malignancies worldwide, accounting for 693,900 deaths in 2012, and the number increases each year.[1] Locally advanced colon cancer (LACC) refers to specific stages during which the tumor is advanced, yet no evidence of metastasis is seen.[2] The standard treatment for LACC is curative resection of the tumor,

[*] *Corresponding author*. Department of Surgical Oncology and General Surgery, The First Affiliated Hospital of China Medical University, Shenyang 110001, PR China. Tel.: +86 24 83283556; fax: +86 24 22703578.
E-mail address: josieon826@sina.cn (Z. Wang).

[1] Xi Zhong and Zhexu Guo contribute equally to this work.

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and postoperative adjuvant chemotherapy (CT) has become a routine procedure that is beneficial to these patients, with good increases in survival.[3] In recent years, racial/ethnic disparities have been investigated, and some studies have demonstrated that African Americans (blacks) are at higher risk of advanced stage colorectal cancer and more likely to have poor prognosis compare with Caucasian Americans (whites).[4-6] Investigators have studied various factors regarding socioeconomic status (SES) based on real world data acquired from Surveillance, Epidemiology, and End Results (SEER) cancer registry–Medicare linked databases to try to explain this racial/ethnic disparity. They highlight that whites, who are more affluent than other races/ethnicities, have more opportunities to consult doctors and receive better and more timely treatments from more experienced physicians.[7-10] However, few studies have adjusted for SES and have focused on potential relationships between racial/ethnic differences and adjuvant CT regimens, which are important for standard care of LACC patients after surgical resection, and how this may influence survival outcomes on a SEER-Medicare basis.

Although race/ethnicity are often considered as social constructs, neglecting their biological properties, several previous studies have demonstrated that significant genetic differences exist between races/ethnicities, some of which are associated with the metabolism of common chemotherapeutic agents such as fluorouracil (5-FU), oxaliplatin, and irinotecan.[11-14] While reporting several genetic differences between black and white patients, Sanoff *et al.*[11] showed that black patients had lower objective response rates and fewer severe adverse effects than whites. However, the genotype-race associations did not contribute to the racial/ethnic disparity in drug efficacy and toxicity. Mack *et al.*[15] observed that black patients had potentially better survival than white patients when receiving oxaliplatin-containing regimens based on SEER-Medicare databases. However, this differential efficacy of oxaliplatin-containing regimens was not significant and therefore cannot fully account for the previously reported racial disparities in colon cancer (CC) survival.

In this study, we explored underlying associations between racial/ethnic disparities and chemotherapeutic regimens in LACC patients using abundant data acquired from SEER-Medicare linked databases to aid in selecting optimal treatments for people from different races/ethnicities in this era of precision medicine.

Methods

Data sources

Data for this population-based retrospective study were from SEER-Medicare linked databases.[16] The Permission to access the research data file in SEER-Medicare program was obtained by the authors (reference no. D6-MEDIC-821). All data were masked and no protected health information could be linked to individual patients. The study was approved by the Institutional Review Board of the First Hospital of China Medical University (reference no. [2012] 96). The National Cancer Institute SEER program covers ~28% of the US population and accumulates extensive data on cancer patients, providing clinical and demographic information that is critical for oncological research. Medicare provides insurance for ~97% of the population aged >65 y in the United States. SEER-Medicare linked databases are constructed by linking Medicare claims with SEER data and have been extensively used to obtain crucial information on patient demographics, cancer characteristics, health care utilization, and comorbidity.[17]

Study population

This study included patients, aged ≥66 y, diagnosed with American Joint Committee on Cancer (AJCC) stage II or III CC (together termed as LACC) between 1992 and 2009, who underwent surgical resection with or without follow-up adjuvant therapy. Individuals that received neoadjuvant therapy were excluded because of the small sample size and likely misclassification of stage IV patients as stage III. Patients were also excluded if they (1) had prior nonrectal cancer, (2) were diagnosed with another malignancy 1 y after the date of LACC diagnosis, or (3) had membership in a Medicare-sponsored health maintenance organization or lack of enrollment in Medicare Parts A and B from 12 mo preceding diagnosis to 12 mo after diagnosis. A total of 55,334 individuals were included, of which 47,328 were whites (non-Hispanic white), 4543 were blacks, 1650 were Asians, 713 were Hispanics (Hispanic white), and 1100 were other minorities including American Indians and Pacific Islanders.

Definition of cohorts

We divided the total population into three cohorts according to their adjuvant CT regimen: no-CT, fluoropyrimidine, and fluoropyrimidine with oxaliplatin. These comprise the recommended adjuvant CT regimens for LACC patients in the National Comprehensive Cancer Network guidelines.[18] Fluoropyrimidine with oxaliplatin was defined as the simultaneous presence of 5-FU or capecitabine and oxaliplatin claims and absence of any other drug claims. Fluoropyrimidine was defined as the presence of only 5-FU or capecitabine claims. The detailed drug codes based on National Drug Code and Health Care Financing Administration Common Procedure Coding System have been reported previously.[19]

Study variables

Overall mortality refers to death from any cause during follow-up. Individuals who were still alive at their last follow-up were censored. Survival was calculated in month from the date of diagnosis to the date of death or last follow-up. Race and regimens of adjuvant CT were the primary covariates of interest, and other demographic or clinical variables such as age at diagnosis, year of diagnosis, sex, marital status, state, residence location, median income of households (income hereafter), educational level of communities (education hereafter), Medicare and Medicaid Services Hierarchical Condition Category (HCC hereafter), AJCC stage of CC, tumor size, tumor grade, tumor histology, number of lymph nodes examined, and comorbidity were also obtained from SEER-Medicare linked databases. Continuous variables including