

Geographic and Demographic Disparities in Colorectal Cancer: A Population-Based Study Using National Cancer Database

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RESEARCH ARTICLE

Geographic and Demographic Disparities in Colorectal Cancer: A National Cancer Database Analysis

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Abstract

Background and objectives: Area of residence may adversely affect survival and outcomes in many cancers. The objective of this study was to evaluate the impact of geographical and demographic disparities on survival of patients with colorectal cancer.

Materials and methods: Data were obtained from the National Cancer Database (NCDB) colon, rectosigmoid, and rectal datasets. Patients were categorized by area of residence, namely, metropolitan (MA), urban (UA), or rural (RA). Sociodemographic and tumor-related data were collected and analyzed to evaluate variables affecting overall survival (OS).

Results: In total, 973,139 patients between 2004 and 2013 were included in the study, of which 83%, 15%, and 2% were MA, UA, and RA residents, respectively. RA and UA patients were mostly white male with low income and no comorbidities. In univariate analysis, OS was worse for RA (hazard ratio [HR] 1.10) and UA (HR 1.06) colorectal cancer patients than that for MA colorectal cancer patients. In multivariate analysis revealed significant association between OS and geographic residence, with worse OS for RA (HR 1.02, $p = 0.04$) and UA (HR 1.01, $p = 0.003$) patients. Black (HR 1.14) and Native American (HR 1.17) patients had worse outcomes, while Asians (HR 0.8), women (HR 0.88), and patients with higher income had improved OS (HR 0.88).

Conclusion: The differences in the OS for RA and UA patients with colorectal cancer were significantly driven by economic disparity. Area of residence represents an important factor independently limiting access to care, particularly in geographically isolated individuals.

Keywords: Colorectal cancer, National cancer database (NCDB), Sociodemographic disparities, Urban-rural disparity, Overall survival

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1. Introduction

Colorectal cancer (CRC) is the most common type of gastrointestinal cancer and the second most common cause of cancer-related mortality in the United States (US) [1]. It is estimated that 4.6% of men (1 in 22) and 4.2% of women (1 in 24) will be diagnosed with CRC in their lifetime. Fortunately, there has been a significant decline in the mortality from CRC over the past few decades, likely owing to widespread use of screening, advanced understanding of the biology, and improved therapeutic approaches. Screening tools such as colonoscopy, sigmoidoscopy, and fecal occult blood test (FOBT) aid in early diagnosis among asymptomatic patients and with timely intervention, result in reduction of overall morbidity and mortality [2]. However, recent literature suggests an increased incidence and subsequent mortality from CRC in rural US populations, owing to lesser use of cancer screening and access to cancer care [3–5]. Differences in community participation at large may reflect disparities in resource availability, population education, and various socioeconomic factors [6]. Using a large national database, the National Cancer Database (NCDB), we sought to examine outcomes for patients with CRC based upon geographic characteristics, namely, the metropolitan versus the non-metropolitan population. Major goals were to validate differences in outcomes but also to evaluate factors that may drive these differences in outcomes, including cancer characteristics (histologic features, stage at diagnosis), treatment components, and demographics.

2. Materials and methods

Patients in the hospital-based NCDB diagnosed with CRC between 2004 and 2013 were included for analysis. The NCDB is a clinical oncology, hospital-based registry with datapoints on more than 70% of all newly diagnosed cancer patients across the country [7]. Individuals were excluded from the analysis if they were reported twice, owing to ≥ 1 colon or rectal cancer diagnosis. We collected data on tumor, nodes, and metastases (TNM) stage (I to IV, or unknown), in accordance with the stage categories by the American Joint Committee on Cancer (AJCC), and included patients from all stages.

In our team's previous works, we had pointed out the role of urban-rural disparities in varying survival outcomes in patients with neuroendocrine tumors and gastric cancers [8,9]. However, for the purpose of survival outcomes analysis in this study, the patients were divided into three categories on

Abbreviations:

| | |
|------|---------------------------------------------|
| MA | Metropolitan area |
| UA | Urban area |
| RA | Rural area |
| OS | Overall survival |
| NCDB | National Cancer Database |
| CRC | Colorectal cancer |
| FOBT | Fecal occult blood test |
| TNM | Tumor, nodes, and metastases |
| AJCC | American Joint Committee on Cancer |
| RUCC | Rural – urban continuum code |
| OMB | Office of management and budget |
| HR | Hazard ratio |
| CI | Confidence interval |
| CCI | Charlson comorbidity index |
| SEER | Surveillance, Epidemiology, and End Results |
| TNI | Tailored navigational intervention |

the basis of the area of the residence, namely, metropolitan (MA), urban (UA), or rural (RA), using the Rural-Urban Continuum Code (RUCC) available in the NCDB [10]. The Office of Management and Budget (OMB) classifies RUCC into metropolitan counties, based on the population size of their metro area, and non-metropolitan counties by adjacency to a metro area and degree of urbanization [11]. MA included counties with a population of 250,000 or above (RUCC 1–3). For this study, we divided the non-metropolitan areas into UA or RA. UA was defined as a county with population of 20,000 or more individuals that was adjacent to a metro area (RUCC 4). RA was defined as a county with a population of less than 20,000 or greater than 20,000 individuals but not being located adjacent to a metro area (RUCC 5–9). Data on income were collected; as the upper quartile of income in the US has increased over time, the definition shifted in cases drawn from later time points (after 2007) where the upper quartile was represented as $\geq \$63,000$ as opposed to $\geq 46,000$ for pre-2008 cases. Here, we divided patients based upon upper quartile of income (>46 K or >63 K) versus lesser income (<46 K or <63 K).

We analyzed the NCDB data for patients with CRC based on various socio-demographic factors, including age, sex, ethnicity, insurance status, marital status, residence (MA vs. UA vs. RA), and tumor-related factors (grade, histology, stage, and primary site). Pearson Chi-square test (for categorical responses) and Kruskal–Wallis test (for ordinal responses) were used to assess the associations between various socio-demographic and tumor-specific characteristics, and the area of residence. Estimation of overall survival (OS), defined by the time from diagnosis of CRC to death due to any

cause, was the primary endpoint of the study. Univariate and multivariable cox proportional hazard models were used, after adjusting for age, sex, ethnicity, marital status, insurance status, area of residence, grade, tumor location, stage, and year of diagnosis, to evaluate OS. Result estimates were expressed as hazard ratio (HR) with 95% confidence interval (CI). Long-term survival evaluation was performed utilizing Kaplan–Meier method, with comparisons based on the log-rank test. Baseline characteristics of patients and outcomes were compared between the individual groups, and $p < 0.05$ was used to depict statistical significance. Analyses were performed on the entire population as well as separately considering the site of origin, cases of colon cancer versus rectal cancer. Statistical Analysis Software (SAS version 9.4) was used to perform all statistical analyses.

3. Results

A total of 973,139 patients between 2004 and 2013 were included in the study, including 83% patients residing in MA, 15% from UA, and 2% from RA. Baseline demographic and clinical characteristics of all patients with CRC in the dataset are presented in [Supplementary Table 1](#) and those with specific diagnosis of rectal and colon carcinoma are presented in [Table 1](#) and [Table 2](#), respectively. Overall,

RA and UA patients were more likely to be white as compared to MA patients (91.3 vs 90.7% vs 81.9%). In comparison with MA patients, RA and UA patients were slightly more likely to be male (50.6% vs 54.3% vs 52.9%) and less likely to have no comorbidities (71.7% vs 69.3% vs 69.7%). RA and UA patients were much more likely to have lower income (<46 K or <63 K) than MA patients (96.5% vs 95.6% vs 64.1%). More patients in the MA were privately insured, and a greater number of patients in the RA had a government-issued health insurance. Uninsured rates were low (3.3%) and similar among all groups. These findings were similar when patients with rectal and colon cancers were separately evaluated, as shown in [Tables 1 and 2](#). Subgroup analysis among patients with rectal cancer revealed an overall male preponderance across all areas of residence (58.1% vs 41.9%, $p < 0.001$); a slight skewing toward the female sex was noted in the subgroup analysis among those with colon cancer (51.6% vs 48.4%, $p < 0.001$).

Statistically significant differences were observed in tumor-related factors among different groups, but very small differences in TNM stages were noted. Pathologic Stage IV diagnoses were less common in MA (11.4%) as compared to those in RA and UA groups (12.4% and 12.3%, respectively). The percentage of positive margin resections was higher

Table 1. Demographic and clinical characteristics of patients with rectal cancer residing in metro, urban, and rural areas.

| | Metro | Urban | Rural | <i>p</i> -Value |
|------------------------------|----------------|---------------|-------------|-----------------|
| Count, N (%) | 170,236 (82.4) | 31,859 (15.4) | 4540 (2.2) | |
| Age, median (range in years) | 64 (40–90) | 65 (40–90) | 66 (40–90) | <0.01 |
| Race | | | | |
| White (%) | 140,420 (82.5) | 29,125 (91.4) | 4110 (90.5) | <0.01 |
| Black (%) | 19,652 (11.5) | 1815 (5.7) | 271 (6) | |
| Native American (%) | 397 (0.2) | 327 (1) | 97 (2.1) | |
| Asian (%) | 6460 (3.8) | 190 (0.6) | 9 (0.2) | |
| Other (%) | 3307 (2) | 402 (1.3) | 53 (1.2) | |
| Sex | | | | |
| Male (%) | 97,891 (57.5) | 19,308 (60.6) | 2774 (61.1) | <0.01 |
| Female (%) | 72,345 (42.5) | 12,551 (39.4) | 1766 (38.9) | |
| Median household income | | | | |
| <46 K or 63 K | 109,620 (64.4) | 30,468 (95.6) | 4377 (96.4) | <0.01 |
| >46 K or 63 K | 60,308 (35.4) | 1312 (4.1) | 141 (3.1) | |
| Unknown | 308 (0.2) | 79 (0.2) | 22 (0.5) | |
| TNM staging (Clinical) | | | | |
| 0 (%) | 8671 (5.1) | 1090 (3.4) | 152 (3.3) | <0.01 |
| I (%) | 28,974 (17.0) | 5176 (16.2) | 689 (15.2) | |
| II (%) | 26,644 (15.7) | 5757 (18.1) | 866 (19.1) | |
| III (%) | 25,846 (15.2) | 5076 (15.9) | 684 (15.1) | |
| IV (%) | 20,278 (11.9) | 3867 (12.2) | 552 (12.2) | |
| Unknown or not applicable | 59,791 (35.1) | 10,887 (34.2) | 1597 (35.1) | |
| TNM staging (Pathological) | | | | |
| 0 (%) | 7398 (4.6) | 1107 (3.6) | 159 (3.6) | <0.01 |
| I (%) | 32,508 (20) | 6263 (20.6) | 933 (21.4) | |
| II (%) | 20,120 (12.4) | 4288 (14.1) | 584 (13.4) | |
| III (%) | 24,872 (15.3) | 5302 (17.5) | 764 (17.5) | |
| IV (%) | 10,335 (6.4) | 2044 (6.7) | 322 (7.4) | |
| Unknown or not applicable | 67,309 (41.4) | 11,369 (37.4) | 1600 (36.7) | |
| Insurance | | | | |
| Not insured (%) | 6753 (4) | 1330 (4.2) | 229 (5.0) | <0.01 |
| Insured (%) | 159,861 (93.9) | 29,829 (93.6) | 4206 (92.6) | |
| Unknown (%) | 3622 (2.1) | 700 (2.2) | 105 (2.3) | |

Table 2. Demographic and clinical characteristics of patients with colon cancer residing in metro, urban, and rural areas.

| | Metro | Urban | Rural | p-Value |
|------------------------------|----------------|---------------|---------------|---------|
| Count, N (%) | 562,076 (83.7) | 95,600 (14.2) | 13,778 (2.1) | |
| Age, median (range in years) | 71 (40–90) | 70 (40–90) | 71 (40–90) | <0.01 |
| Race | | | | |
| White (%) | 458,676 (81.6) | 86,387 (90.4) | 12,599 (91.4) | <0.01 |
| Black (%) | 77,307 (13.8) | 7258 (7.6) | 856 (6.3) | |
| Native American (%) | 842 (0.1) | 600 (0.6) | 199 (1.4) | |
| Asian (%) | 3242 (0.6) | 27 (0.0) | 2 (0.0) | |
| Other (%) | 22,009 (3.9) | 1328 (1.4) | 122 (0.9) | |
| Sex | | | | |
| Male (%) | 270,504 (48.1) | 47,633 (49.8) | 7101 (51.5) | <0.01 |
| Female (%) | 291,572 (51.9) | 47,967 (50.2) | 6677 (48.5) | |
| Median household income | | | | |
| <46 K or 63 K | 359,982 (64.1) | 91,225 (95.6) | 13,254 (96.6) | <0.01 |
| >46 K or 63 K | 201,197 (35.9) | 4167 (4.4) | 471 (3.4) | |
| Unknown | 0 (0) | 0 (0) | 0 (0) | |
| TNM staging (Clinical) | | | | |
| 0 (%) | 26,294 (4.7) | 3609 (3.8) | 466 (3.4) | <0.01 |
| I (%) | 66,208 (11.8) | 11,614 (12.1) | 1540 (11.2) | |
| II (%) | 48,797 (8.7) | 9051 (9.5) | 1178 (8.5) | |
| III (%) | 33,149 (5.9) | 6143 (6.4) | 796 (5.8) | |
| IV (%) | 73,687 (13.1) | 13,195 (13.8) | 1769 (12.8) | |
| Unknown or not applicable | 313,895 (55.8) | 51,978 (54.4) | 8029 (58.3) | |
| TNM staging (Pathological) | | | | |
| 0 (%) | 26,289 (4.7) | 3759 (4) | 541 (4) | <0.01 |
| I (%) | 98,627 (17.9) | 16,626 (17.8) | 2418 (17.9) | |
| II (%) | 130,529 (23.8) | 22,529 (24.2) | 3432 (25.4) | |
| III (%) | 126,777 (23.1) | 22,311 (23.9) | 3296 (24.4) | |
| IV (%) | 70,184 (12.8) | 13,297 (14.3) | 1855 (13.7) | |
| Unknown or not applicable | 97,124 (17.7) | 14,697 (15.8) | 1969 (14.6) | |
| Insurance | | | | |
| Not insured (%) | 16,726 (3.0) | 3038 (3.2) | 407 (3.0) | <0.01 |
| Insured (%) | 535,837 (95.4) | 90,784 (94.9) | 13,116 (95.2) | |
| Unknown (%) | 9513 (1.6) | 1778 (1.9) | 255 (1.8) | |

in MA (22.2%) group than in RA and UA groups (20.5% and 21.2%, respectively). Hospital readmission within 30 days of surgery was not meaningfully different between groups. A significant difference was also observed in 30- and 90-day post-operative mortality rates (RA, 3.8% and 6.5%; UA, 3.3% and 6.1%; MA, 3.2% and 5.9%, respectively). We further separately assessed findings for colon and rectal cancers. While the colon cancer data mirrored the overall data, post-operative mortality rates were not different for patients with rectal cancer. Other trends were similar between rectal and colon cancer patients.

In the univariate analysis, OS was worse for RA (hazard ratio [HR] 1.10) and UA (HR 1.06) patients than for MA patients. Of the additional associations analyzed, age, sex, race, income, insurance status, Charlson Comorbidity Index (CCI) > 1, grade, stage, and tumor primary site were significantly related to survival (Table 2). The strongest associations were seen with clinical stage IV disease (HR 7.13). Consistent effects were observed within colon and rectal cancers, although the outcomes appeared worse among individuals with rectal cancer from RA group (HR 1.15) than among individuals from MA group when considering geography.

Table 3. Multivariate Cox proportional hazard regression model highlighting OS in rectal cancer patient population.

| | Hazard ratio | 95% Confidence interval (CI) | p-Value |
|----------------------------------------------|--------------|------------------------------|---------|
| Rural vs. Metropolitan | 0.99 | 0.95–1.04 | 0.79 |
| Urban vs. Metropolitan | 0.99 | 0.97–1.01 | 0.33 |
| Female vs. male | 0.88 | 0.87–0.90 | <0.001 |
| Charlson Comorbidity Score (≥1 vs. none) | 1.29 | 1.27–1.31 | <0.001 |
| Race | | | |
| Black vs. White | 1.14 | 1.11–1.17 | <0.001 |
| Asian vs. White | 0.81 | 0.77–0.85 | <0.001 |
| Native American vs. White | 1.27 | 1.14–1.43 | <0.001 |
| Insurance status | | | |
| Govt vs. Uninsured | 0.74 | 0.71–0.77 | <0.001 |
| Private vs. Uninsured | 0.60 | 0.58–0.62 | <0.001 |
| Income > \$46k or \$63k vs. < \$46k or \$63k | 0.87 | 0.85–0.88 | <0.001 |
| Clinical stage 1 vs. 0 | 1.15 | 1.09–1.21 | <0.001 |
| Clinical stage 2 vs. 0 | 1.55 | 1.48–1.63 | <0.001 |
| Clinical stage 3 vs. 0 | 1.59 | 1.51–1.68 | <0.001 |
| Clinical stage 4 vs. 0 | 6.23 | 5.93–6.55 | <0.001 |

Table 4. Multivariate Cox proportional hazard regression model highlighting OS in colon cancer patient population.

| | Hazard ratio | 95% Confidence interval (CI) | p-value |
|-------------------------------------------------|--------------|------------------------------|---------|
| Rural vs. Metropolitan | 1.03 | 1.00–1.06 | 0.02 |
| Urban vs. Metropolitan | 1.02 | 1.01–1.03 | 0.337 |
| Female vs. male | 0.88 | 0.87–0.89 | <0.001 |
| Left vs. Right colon | 0.97 | 0.97–0.98 | <0.001 |
| NOS vs. Right colon | 1.34 | 1.31–1.36 | <0.001 |
| Charlson Comorbidity Score (≥ 1 vs. none) | 1.24 | 1.23–1.25 | <0.001 |
| Race | | | |
| Black vs. White | 1.14 | 1.13–1.15 | <0.001 |
| Asian vs. White | 0.78 | 0.73–0.84 | <0.001 |
| Native American vs. White | 1.13 | 1.04–1.22 | <0.001 |
| Insurance status | | | |
| Govt vs. Uninsured | 0.76 | 0.74–0.78 | <0.001 |
| Private vs. Uninsured | 0.68 | 0.66–0.69 | <0.001 |
| Income > \$46k or \$63k vs. < \$46k or \$63k | 0.88 | 0.87–0.89 | <0.001 |
| Clinical stage 1 vs. 0 | 1.40 | 1.36–1.44 | <0.001 |
| Clinical stage 2 vs. 0 | 1.75 | 1.70–1.80 | <0.001 |
| Clinical stage 3 vs. 0 | 1.86 | 1.81–1.92 | <0.001 |
| Clinical stage 4 vs. 0 | 4.34 | 4.22–4.46 | <0.001 |

Table 5A & B. The overall survival estimates from the NCDB for rectal and colon cancer patients.

| Strata | 3-yr survival rate (95% CI) | 5-yr survival rate (95% CI) | Median survival (95% CI) | Median follow-up (Range) |
|--------------|-----------------------------|-----------------------------|--------------------------|--------------------------|
| Total | 0.69 (0.69, 0.70) | 0.58 (0.58, 0.59) | 84.8 (83.8, 86.0) | 61.0 (0.0, 131.5) |
| Metropolitan | 0.70 (0.69, 0.70) | 0.59 (0.59, 0.59) | 87.3 (86.1, 88.5) | 60.9 (0.0, 131.4) |
| Urban | 0.68 (0.68, 0.69) | 0.57 (0.56, 0.57) | 76.6 (74.8, 78.8) | 61.5 (0.0, 131.5) |
| Rural | 0.67 (0.66, 0.69) | 0.53 (0.52, 0.55) | 68.9 (64.0, 74.4) | 59.8 (0.0, 131.0) |
| Strata | 3-yr survival rate (95% CI) | 5-yr survival rate (95% CI) | Median survival (95% CI) | Median follow-up (Range) |
| Total | 0.64 (0.63, 0.64) | 0.53 (0.53, 0.53) | 69.2 (68.8, 69.7) | 62.0 (0.0, 133.6) |
| Metropolitan | 0.64 (0.64, 0.64) | 0.54 (0.54, 0.54) | 71.9 (71.4, 72.4) | 62.2 (0.0, 133.6) |
| Rural | 0.62 (0.61, 0.63) | 0.51 (0.50, 0.52) | 62.6 (60.2, 65.6) | 61.9 (0.0, 131.6) |
| Urban | 0.62 (0.62, 0.63) | 0.51 (0.51, 0.52) | 63.9 (62.9, 65.2) | 61.4 (0.0, 131.5) |

The multivariate cox proportional hazard regression model identified multiple factors that were independent predictors of OS. Factors associated with overall OS within both the colon and rectal cancer subgroups were older age, male sex, insurance status (uninsured), lower income, comorbidities (CCI >1), high histologic grade, right-sided primary tumor location, and higher clinical or pathologic stage (Tables 3 and 4). Non-metropolitan geographic residence was significantly associated with survival in the overall population (Supplementary Table 2) and within the colon cancer subpopulation (Table 4), although this difference did not persist within rectal cancer as a sub-site (Table 3). Among the colon cancer subgroup, the geographical disparity was noticeable only between patients from RA and MA groups but not between those from UA and MA groups. When considering race, the outcomes were worse for Black ($p < 0.001$) and Native American ($p < 0.001$) patients but better for Asian patients ($p < 0.001$) than for White patients among both subgroups.

Survival estimates in Kaplan–Meier analysis revealed an unadjusted median OS of 73.3 months overall, 75.9 months for patients from MA, 68.2

months for UA, and 64.5 months from RA. With a median follow-up range of 62 months, the 5-year survival rates were 55% (MA), 53% (UA), and 52% (RA). The unadjusted median OS was 71.9, 63.9, and 62.6 months for colon cancer patients and 87.3, 76.6, and 68.9 months for rectal cancer patients from MA, UA, and RA, respectively. OS rates (3-year, 5-year, and median) are summarized in Table 5A for patients with rectal cancer and Table 5B for patients with colon cancer. Similarly, Kaplan–Meier curves of the OS estimates from the NCDB for both patient subgroups are presented in Figs. 1 and 2.

4. Discussion

The aim of our study was to assess and highlight CRC survival disparities between metropolitan and non-metropolitan communities nationwide. We observed worse survival outcomes amongst non-metropolitan populations (UA and RA) in univariate analysis. Multivariate analysis revealed significant association between OS and geographic residence, age, sex, race, income, insurance status, presence of comorbidities, primary tumor site, stage, and grade. Of importance, we demonstrated that geographic

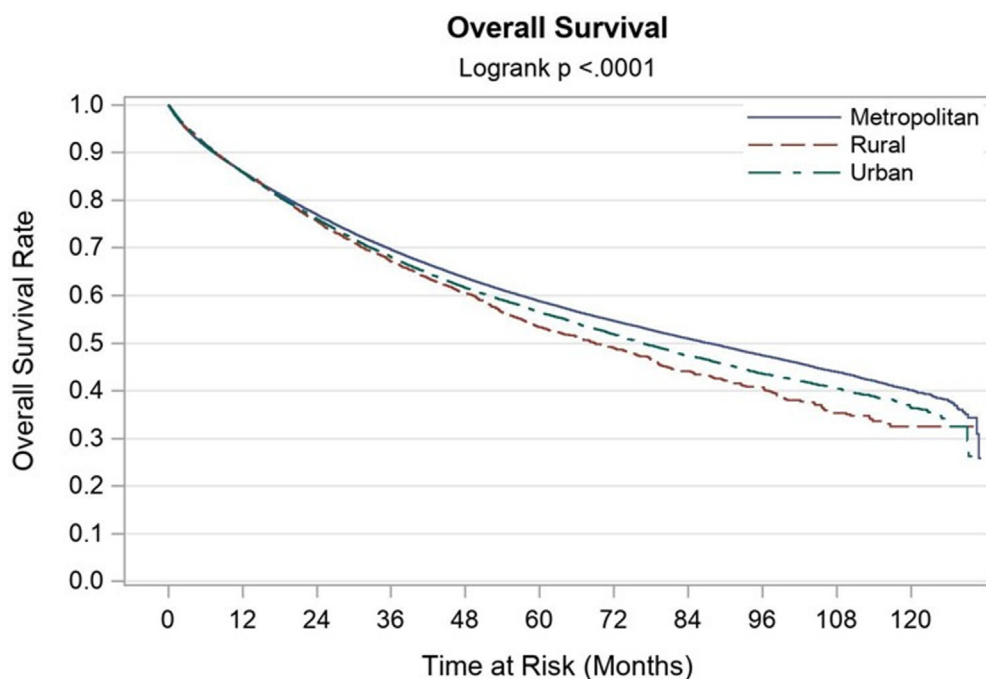


Fig. 1. Kaplan–Meier analysis of overall survival estimates from the NCDB for patients with rectal cancer. (Color should be used for figures in print).

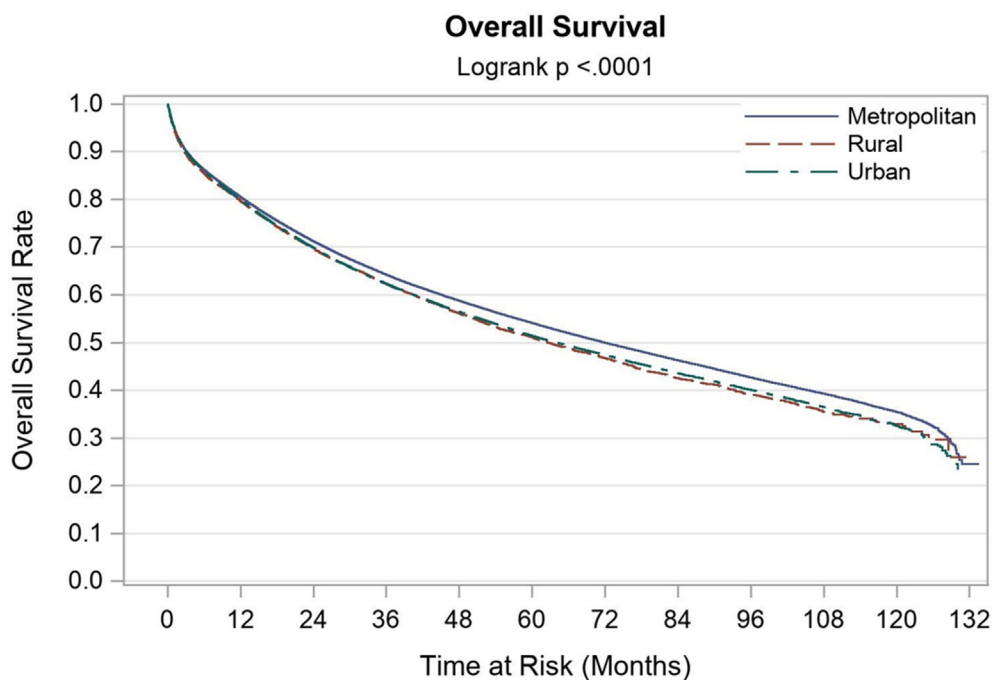


Fig. 2. Kaplan–Meier analysis of overall survival estimates from the NCDB for patients with colon cancer. (Color should be used for figures in print).

residence was associated with outcome, after adjusting for multiple relevant covariates; however, the independent effect appears to be relatively small with a HR of 1.02 for rural residence and 1.01 for urban residence.

We observed considerable disparities within non-metropolitan populations (UA and RA), with markedly higher proportions of patients having

lower income and lesser rates of private insurance. There were fewer female and more patients with comorbidities in non-metropolitan areas. Given the worse outcomes observed for patients with lower income, men, and those with comorbidities, it seems plausible that this accounts for much of the difference seen between the metropolitan and non-metropolitan populations. Very small but significant

differences in post-operative mortality were also observed, favoring patients originating from metropolitan areas. Racial differences were also detected, although the impact is less straightforward. Within non-metropolitan areas, the population was skewed; there was a higher proportion (>90%) of White patients and a lower prevalence of Black and Asian patients, but a higher prevalence of Native-Americans, particularly in the least populated areas (RA). Interestingly, when we separately assessed rectal and colon cancers, non-metropolitan residence did not have an independent effect on survival within rectal cancer patients but maintained an independent association amongst patients with colon cancer (rural, HR 1.03, $p = 0.026$; urban, HR 1.02, $p < 0.001$). The reasons for these differences are unclear, although rectal cancers constituted less than 25% of the cases.

Disparity in cancer incidence is well established among populations defined by age, gender, and race. Recent epidemiological studies on overall cancer incidence and mortality have demonstrated that the incidence of cancer has increased within metropolitan populations as compared to that in non-metropolitan (often referred to as rural) counterparts; however, rates of cancer-related deaths maintain the opposite trend, with increased mortality reported in the non-metropolitan population [6,12,13]. Further, while age-adjusted cancer death rate is decreasing, the degree of decline remains lower in these same non-metropolitan areas (-1.6% per year vs -1.0% per year). A study on the effect of rurality on life expectancy in the US has shown that the gap in life expectancy between residents in large MA and those in small UA and RA has widened over the decades. People in large MA now live 2.4 years longer than people in RA as compared to 4 decades ago when the difference was just 0.4 years [14]. Factors such as higher smoking rates in rural population, greater poverty leading to lack of insurance, poor access to primary care provider, lower cancer screening, individual 'beliefs' and biases around cancer and chemotherapy have been traditionally implicated in the discrepancies in OS rates [15–21]. However, recent studies on disparities in screening methods have shown the gap to be closing between the urban and rural population [22,23]. This may, in part, explain why the OS in patients with CRC when adjusted for known variables in our study was limited between patients from MA, UA, and RA. This is in contrast to the results from previous studies where OS rates were poorer for patients from rural areas than for those from urban areas [24–26].

It is important to note that our study has some limitations. Firstly, this study design is retrospective.

The outcomes may be impacted by selection and misclassification bias. Secondly, we could adjust only for known variables; thus, unknown variables may introduce further bias and additionally influence outcomes. Thirdly, data on cancer recurrence are not provided in the NCDB. For this reason, we could not discriminate between cancer-related and non-cancer-related mortality differences in these populations. We did not consider treatment modalities, such as radiation and adjuvant or neoadjuvant chemotherapy. Additionally, the NCDB does not provide data such as hospital or surgeon-specific case volume, which may also affect outcomes, as seen in some prior studies [27,28]. While differences in practice patterns or access to life-altering therapies may be responsible for these differences, this study was not designed to assess this detail. To our knowledge, this represents one of the largest, all-inclusive studies investigating geographically based disparities pertaining to CRC outcomes within the NCDB. Previous studies conducted in the US primarily evaluated the patients via the SEER registry. In this study, we chose not to utilize the dichotomous metropolitan/non-metropolitan classification system both due to past inconsistency and in attempt to increase granularity. Our findings are consistent with prior studies and further display the geographic disparities linked to worse outcomes. Findings from multivariate analysis suggest that a significant amount of observed disparity may be related to differences in population-level characteristics, including socioeconomic factors (lower income) and increased rates of comorbidities, which can clearly impact access to care and provision of optimal care.

Our study showed that patients from low income-rural areas had worse outcomes, consistent with the results of a previous study where patients from poorer neighborhood with a low annual household income had lower screening rates than the national average. It is not surprising that a much higher incidence and advanced disease were seen at the time of diagnosis [29]. Our study also showed that OS rates were lower in Black patients than in White patients for CRC. This observation aligns with similar results demonstrated by Holowatyj and colleagues in their study where worse survival rates were documented among young Black Americans even among early-stage CRC patients [30]. An interesting approach by Myers and team to improve the colon cancer screening rates among African-Americans in primary care was to employ a tailored navigation intervention (TNI) comprising a preference-based mail-in stool blood test kit or colonoscopy instructions, with telephone navigation and a

reminder. At the end of 6 months, TNI group showed significantly higher adherence to screening than standard single mail kit only group [31]. Other approaches that could further help to close the disparity gap include employing mobile screening units, encouraging community-driven multi-faceted approach, tele-medicine, training and utilizing nurse practitioners and physician assistants to administer home-based chemotherapy, and subsidizing hospitals and providing financial aid to run hospitals in rural and underserved communities [32–34].

5. Conclusion

Achieving equity in health necessitates elimination of systemic disparities in healthcare and fulfilment of the major determinants of health at various levels between socio-demographically different groups. Special attention is warranted toward not only advancing the cancer care services but also putting in concentrated efforts to operate efficiently and make these services amenable to vulnerable communities and reduce the cancer discrepancies. As mentioned earlier, use of screening methods in patients with CRC is instrumental to diminish the mortality rate. Various screening programs employing either the mail-based approach or more “patient-reliant” approach are used to identify high-risk individuals. However,

the effectiveness of these programs is dependent on patient initiation and willingness, capability to collect and return the tests, the knowledge of resources available, skill to request participation, and access to programs.

Disclosure

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Author contributions

(I) Conception and design: TM, RG, NR, EG, SN and PB.

(II) Administrative support: RG, NR, RL, EG, SN and PB.

(III) Provision of study materials or patients: TM, AA, KW, AN, RG, NR and RL.

(IV) Collection and assembly of data: TM, AA, KW, AN, RG, NR, EG, SN and RL.

(V) Data analysis and interpretation: TM, RG, NR, AA, KW, AN, RL, EG, SN and PB.

(VI) Manuscript writing: All authors

(VII) Final approval of manuscript: All authors

Data statement

The datasets generated and/or analyzed during the current study are available in the National Cancer Database (NCDB) public repository and can

Appendix.

Supplementary Table 1. Demographic and clinical characteristics of all patients with colorectal carcinoma residing in metro, urban, and rural areas.

| | | Metro | Urban | Rural | p-Value |
|------------------------------|---------------------------|----------------|----------------|---------------|---------|
| Count, N (%) | | 791,664 (83.4) | 137,929 (14.5) | 19,832 (2.1) | |
| Age, median (range in years) | | 69 (40–90) | 68 (40–90) | 69 (40–90) | <0.01 |
| Race | White (%) | 648,342 (81.9) | 125,082 (90.7) | 18,113 (91.3) | <0.01 |
| | Black (%) | 103,219 (13) | 9669 (7) | 1196 (6) | |
| | Native American (%) | 1369 (0.2) | 1023 (0.7) | 316 (1.6) | |
| | Asian (%) | 10,139 (1.3) | 220 (0.2) | 11 (0.1) | |
| | Other (%) | 28,595 (3.6) | 1935 (1.4) | 196 (1) | |
| Sex | Male (%) | 400,958 (50.6) | 72,994 (52.9) | 10,771 (54.3) | <0.01 |
| | Female (%) | 390,706 (49.4) | 64,935 (47.1) | 9061 (45.7) | |
| Median household income | <46 K or 63 K | 506,745 (64.1) | 131,642 (95.6) | 19,092 (96.5) | <0.01 |
| | >46 K or 63 K | 283,625 (35.8) | 5972 (4.3) | 656 (3.3) | |
| | Unknown | 397 (0.1) | 107 (0.1) | 31 (0.2) | |
| TNM staging (Clinical) | 0 (%) | 37,169 (4.7) | 4991 (3.6) | 651 (3.3) | <0.01 |
| | I (%) | 102,514 (13) | 18,104 (13.1) | 2390 (12.1) | |
| | II (%) | 81,378 (10.3) | 15,971 (11.6) | 2220 (11.2) | |
| | III (%) | 64,436 (8.1) | 12,219 (8.9) | 1612 (8.1) | |
| | IV (%) | 102,320 (12.9) | 18,513 (13.4) | 2560 (12.9) | |
| | Unknown or not applicable | 403,761 (51.0) | 68,115 (49.4) | 10,398 (52.4) | |

(continued on next page)

Supplementary Table 1. (continued)

| | | Metro | Urban | Rural | p-Value |
|----------------------------|---------------------------|----------------|----------------|---------------|---------|
| TNM staging (Pathological) | 0 (%) | 35,763 (4.6) | 5176 (3.9) | 739 (3.8) | <0.01 |
| | I (%) | 141,899 (18.4) | 24,737 (18.5) | 3592 (18.6) | |
| | II (%) | 161,770 (21) | 28,840 (21.6) | 4308 (22.4) | |
| | III (%) | 166,505 (21.6) | 30,299 (22.7) | 4475 (23.1) | |
| | IV (%) | 87,461 (11.4) | 16,630 (12.3) | 2380 (12.3) | |
| | Unknown or not applicable | 176,284 (23) | 28,021 (21) | 3851 (19.8) | |
| Insurance | Not insured (%) | 25,675 (3.3) | 4775 (3.5) | 703 (3.5) | <0.01 |
| | Insured (%) | 751,700 (94.9) | 130,464 (94.5) | 18,742 (94.5) | |
| | Unknown (%) | 14,289 (1.8) | 2690 (2.0) | 387 (2.0) | |
| | | | | | |

Supplementary Table 2. Multivariate Cox proportional hazard regression model highlighting OS in all colorectal carcinoma patient population.

| | Hazard ratio | 95% Confidence interval (CI) | p-value | |
|--------------------------------------------------|---------------------------|------------------------------|-----------|--------|
| Rural vs. Metropolitan | 1.02 | 0.99–1.05 | 0.04 | |
| Urban vs. Metropolitan | 1.01 | 0.99–1.02 | 0.003 | |
| Female vs. Male | 0.88 | 0.87–0.89 | <0.001 | |
| Cancer of left Colon vs. Right colon | 0.98 | 0.97–0.99 | <0.001 | |
| NOS vs. Right Colon | 1.39 | 1.37–1.41 | <0.001 | |
| Rectal vs. Right Colon | 0.96 | 0.95–0.97 | <0.001 | |
| Rectosigmoid vs. Right colon | 1.00 | 0.98–1.01 | 0.738 | |
| Charlson Comorbidity Score (≥ 1 vs. none) | 1.25 | 1.24–1.26 | <0.001 | |
| Race | Black vs. White | 1.14 | 1.13–1.15 | <0.001 |
| | Asian vs. White | 0.80 | 0.77–0.83 | <0.001 |
| | Native American vs. White | 1.17 | 1.10–1.25 | <0.001 |
| | Govt vs. Uninsured | 0.75 | 0.74–0.77 | <0.001 |
| Insurance status | Private vs. Uninsured | 0.65 | 0.64–0.67 | <0.001 |
| Income > \$46 k or \$63 k vs. < \$46 k or \$63 k | 0.88 | 0.87–0.89 | <0.001 | |
| Clinical stage 1 vs. 0 | 1.30 | 1.27–1.33 | <0.001 | |
| Clinical stage 2 vs. 0 | 1.66 | 1.62–1.70 | <0.001 | |
| Clinical stage 3 vs. 0 | 1.75 | 1.70–1.79 | <0.001 | |
| Clinical stage 4 vs. 0 | 4.64 | 4.53–4.75 | <0.001 | |

be accessed upon request through <https://www.facs.org/quality-programs/cancer/ncdb/publicaccess>.

Conflict of interest

None.

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None.

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