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ORIGINAL ARTICLE

Disparity of Colon Cancer Outcomes in Rural America: Making the Case to Travel the Extra Mile

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Abstract

Objectives Rural patients experience disparities in cancer care compared to urban patients. We hypothesized that rural patients with colon cancer who traveled to high-volume centers for treatment have similar survival compared to urban patients who also traveled to high-volume centers to seek treatment for colon cancer.

Methods The National Cancer Database was interrogated for patients treated for stage I–III colon cancer (2004–2015). Travel distance to treatment centers and annual hospital volume were divided into quartiles. Two groups of patients were identified and compared: (1) rural patients who traveled to high-volume hospitals and (2) urban patients who also traveled to high-volume centers. The primary outcome was overall survival (OS).

Results Of 647,949 patients, 634, 447 were urban and 13,502 were rural. Rural patients were more likely to be Caucasian, with lower income, more comorbidities, and be treated at non-academic centers. In multivariable analysis, rural patients had worse OS compared to urban patients (hazard ratio [HR] 1.08; 95% confidence interval [CI] 1.04–1.12; $p = < 0.001$). There were 46,781 (7%) urban patients and 1276 (9%) rural patients who traveled a long distance (median 40 and 108 miles, respectively) to high-volume centers. There was no difference in adjusted OS between urban and rural patients who traveled to high-volume centers for treatment (HR 1.06; 95%CI 0.94–1.20; $p = 0.36$).

Conclusions This nationwide analysis suggests that rural patients with colon cancer experience worse survival than urban patients, but that this disparity might be mitigated by rural patients traveling to high-volume centers for treatment.

Keywords Colon cancer · Disparities · Rural · Urban

Introduction

Colorectal cancer is the third most diagnosed cancer in the USA, with an estimated 140,000 new cases and 51,000 deaths in 2018.[1] Several populations have been identified with worse cancer-related survival, including people with a lower socioeconomic status, who are non-Caucasian, and those who live in rural areas.[2] While urbanization has resulted in a shrinking rural population in America, 18% of Americans still live in rural areas.[3] Rural patients diagnosed with colon cancer have worse survival than urban patients.[2] This disparity likely roots from differences in socioeconomic status, cancer risk factors, stage at presentation, screening, and access to high-volume treatment centers.[2] High-volume colon cancer care has been shown to improve local recurrence and survival compared to low-volume centers.[4–6] We hypothesized that the higher mortality of rural patients with stage I–III colon cancer could be mitigated by travel to a high-volume center for treatment.

Methods

The National Cancer Database (NCDB) is a joint program of the Commission on Cancer (CoC) of the American College of Surgeons and the American Cancer Society. The NCDB is a nationwide, facility-based, comprehensive clinical surveillance dataset that captures 80% of all newly diagnosed cancer in the USA. This study was granted exempt status from the Duke University Institutional Review Board.

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Table 1 Background characteristics of study patients

	Rural ($N = 13,502$)	Urban ($N = 634,447$)	p value
Patient age			
Median	70.0	70.0	0.0001
Q1, Q3	61, 79	59, 79	
Sex			< 0.0001
Male	7100 (52.6%)	310,544 (48.9%)	
Female	6402 (47.4%)	323,903 (51.1%)	
Race			< 0.0001
Black	843 (6.2%)	81,047 (12.8%)	
White	12,336 (91.4%)	524,488 (82.7%)	
Insurance type			< 0.0001
Medicare	8888 (67.1%)	363,694 (58.3%)	
Private	3264 (24.6%)	205,898 (33.0%)	
Medicaid	522 (3.9%)	29,380 (4.7%)	
None	398 (3.0%)	19,989 (3.2%)	
Charlson-Deyo score			< 0.0001
0	9051 (67.0%)	439,302 (69.2%)	
1	3162 (23.4%)	139,849 (22.0%)	
≥2	1289 (9.5%)	55,296 (8.7%)	
Hospital location			< 0.0001
Midwest	5804 (43.8%)	165,973 (26.7%)	
South	5978 (45.2%)	229,727 (37.0%)	
West	1111 (8.4%)	92,193 (14.9%)	
Northeast	344 (2.6%)	132,621 (21.4%)	
Hospital type			< 0.0001
Academic	2148 (16.2%)	168,864 (27.2%)	
Community	2588 (19.6%)	81,627 (13.2%)	
Comprehensive community	8501 (64.2%)	370,023 (59.6%)	
Year of diagnosis			0.0594
2004	1042 (7.7%)	50,602 (8.0%)	
2005	1014 (7.5%)	51,024 (8.0%)	
2006	1069 (7.9%)	51,783 (8.2%)	
2007	1155 (8.6%)	53,208 (8.4%)	
2008	1132 (8.4%)	53,349 (8.4%)	
2009	1166 (8.6%)	52,317 (8.2%)	
2010	1070 (7.9%)	52,348 (8.3%)	
2011	1217 (9.0%)	52,759 (8.3%)	
2012	1085 (8.0%)	53,236 (8.4%)	
2013	1210 (9.0%)	54,334 (8.6%)	
2014	1208 (8.9%)	54,782 (8.6%)	
2015	1134 (8.4%)	54,705 (8.6%)	
Tumor size (cm)			< 0.0001
Median	4.2	4.0	
Q1, Q3	3.0, 6.0	2.8, 6.0	
High tumor grade	2823 (22.9%)	117,909 (20.6%)	< 0.0001
Metastatic disease at diagnosis			0.1106
No	10,759 (79.7%)	509,092 (80.3%)	
Yes	2738 (20.3%)	125,137 (19.7%)	
Clinical stage			0.0457
1	1822 (31.9%)	94,718 (33.7%)	
2	1194 (20.9%)	56,659 (20.2%)	
3	805 (14.1%)	38,875 (13.8%)	
4	1886 (33.0%)	90,892 (32.3%)	

The cohort initially was categorized into two groups: rural and urban. Data about rural-urban continuum were provided in the dataset, using a classification scheme that distinguishes patients' residence counties by the population size, degree of urbanization, and adjacency to a metro area. Rural counties were defined as completely rural or have < 2500 urban population. Urban counties included urban and metropolitan counties. Annual hospital procedure volume was calculated. Travel distance to treatment centers and annual hospital volume were divided into quartiles.

We then created two groups by overlaying rural vs. urban status with top quartile of each of annual hospital volume and travel distance: (1) rural patients who traveled to high-volume centers (RT) and (2) urban patients who traveled to high-volume centers (UT).

Statistical Analysis

Baseline characteristics were reported using frequencies and proportions for categorical variables. Descriptive data were compared across groups using the Wilcoxon rank sum test for continuous variables and Pearson Chi-square or Fisher's exact tests for categorical variables.

Overall survival was defined from the time of diagnosis to time of death or last follow-up. Survival time was censored for

Table 2 Surgery and hospitalization characteristics of study patients

	Rural ($N = 13,502$)	Urban ($N = 634,447$)	p value
Pathological stage			0.0077
	1949 (14.4%)	104,629 (16.5%)	
1	2731 (23.6%)	132,409 (25.0%)	
2	3427 (29.7%)	156,151 (29.5%)	
3	3529 (30.5%)	157,236 (29.7%)	
4	1866 (16.2%)	84,022 (15.9%)	
Time to surgery (days)			< 0.0001
Median	15.0	17.0	
Q1, Q3	5.0, 29.0	6.0, 32.0	
Extent of surgery			0.2197
Segmental resection	10,436 (97.0%)	477,441 (97.1%)	
Total proctocolectomy	44 (0.4%)	2445 (0.5%)	
Total colectomy	274 (2.5%)	11,660 (2.4%)	
Minimally invasive technique			< 0.0001
No	3029 (55.3%)	130,066 (50.1%)	
Yes	2446 (44.7%)	129,442 (49.9%)	
Number of lymph nodes removed			< 0.0001
≥ 12	8955 (77.7%)	421,260 (79.5%)	
< 12	2571 (22.3%)	108,395 (20.5%)	
Surgical margins			0.1937
Negative	10,952 (92.8%)	508,142 (93.1%)	
Positive	855 (7.2%)	37,853 (6.9%)	
Length of stay			0.0003
Median	6.0	6.0	
Q1, Q3	5.0, 9.0	4.0, 8.0	
30-day readmission			0.5604
No	12,585 (95.1%)	587,388 (95.0%)	
Yes	652 (4.9%)	31,197 (5.0%)	
90-day mortality			0.0009
No	10,141 (92.4%)	471,468 (93.2%)	
Yes	833 (7.6%)	34,261 (6.8%)	
Adjuvant chemotherapy			0.0162
No	7755 (68.8%)	363,395 (69.8%)	
Yes	3524 (31.2%)	157,159 (30.2%)	

patients alive at the end of the study period. Estimates of overall survival proportions were computed using the Kaplan-Meier method, and survival distributions were compared across groups using the log-rank test. Cox proportional hazards modeling was employed to examine adjusted overall survival difference. The multivariable Cox models used patient- and tumor-related variables deemed a priori to be clinically important to survival and included patient age, sex, race, insurance status, Charleson-Deyo comorbidity index, pathologic stage, extent of surgery, and receipt of adjuvant therapy.

A two-sided p value of < 0.05 indicates statistical significance. All statistical analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC).

Results

Cohort Characteristics

A total of 647,949 patients were included: 634,447 (98%) patients in the urban group and 13,502 (2%) patients were in the rural group. Compared with urban patients, rural patients were more often male, White, have Medicare insurance, with comorbidities, treated at non-academic centers, and sought treatment in the Midwest or South (all $p < 0.05$) (Table 1). Rural patients had similar length of hospitalization and 30-day readmission, but experienced higher 90-day mortality and were less likely to have > 12 nodes removed during surgery (Table 2).

Survival Analysis

Median follow-up time was 37 months (range 1–160 months). Overall survival was compromised for rural patients at both the 5- and 10-year marks (52.3% vs. 54.3% and 34.7% vs. 37.2%, respectively; $p < 0.0001$) (Fig. 1a). After adjustment, overall survival remained compromised for rural patients (hazard ratio (HR): 1.08; 95% CI 1.04 to 1.12; $p < 0.0001$) (Fig. 2a).

Effect of Traveling to High-Volume Centers

Among the rural group, 9% ($n = 1276$) traveled to high-volume centers for surgical treatment, while 7% ($n = 46{,}781$) of urban patients traveled to high-volume centers. Among patients who traveled the furthest, the median travel distance was 40 miles and 108 miles for urban and rural patients, respectively. Compared with urban patients who traveled, rural patients who traveled were more often older and had comorbidities (all $p < 0.01$) (Table 3). Overall survival at 10 years was similar for rural and urban patients who traveled to high-volume centers for surgery (38.9% vs. 39.5%, respectively; $p = 0.17$) (Fig. 1b). Adjusted survival was also similar between groups (HR: 1.06; 95% CI 0.94 to 1.20; $p = 0.36$) (Fig. 2b).

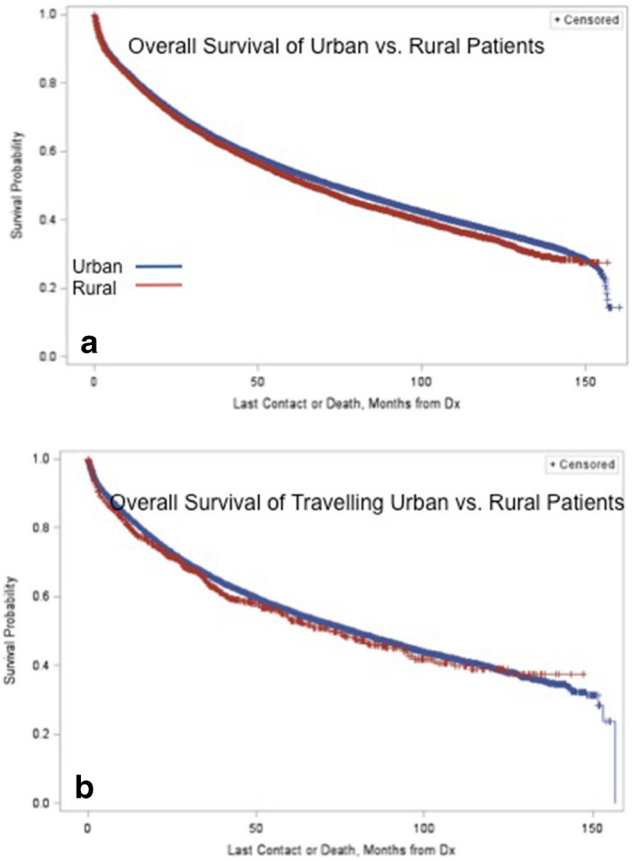

Fig. 1 Kaplan-Meier survival curves comparing survival between **a** urban and rural patients with colon cancer and **b** urban and rural patients who traveled to a high-volume center for treatment

Discussion

In this nationwide study comparing outcomes of rural patients treated for colon cancer with urban patients, we found that rural patients had worse overall survival even after adjustment for patient and tumor characteristics. However, rural patients who traveled a great distance to a high-volume center for treatment had similar survival compared to urban patients who also traveled far to a high-volume center. Therefore, the survival disadvantage of rural living is mitigated with travel to high-volume centers.

Rural patients with colon cancer had worse overall survival compared to urban patients. Rural patients are more likely to present at a more advanced pathologic stage,[7–11] smoke,[12,13] be more obese, have lower socioeconomic status,[11,14], and have worse health literacy than urban patients.[15–17] Rural patients also experience barriers in access to healthcare. For instance, a cross-sectional study

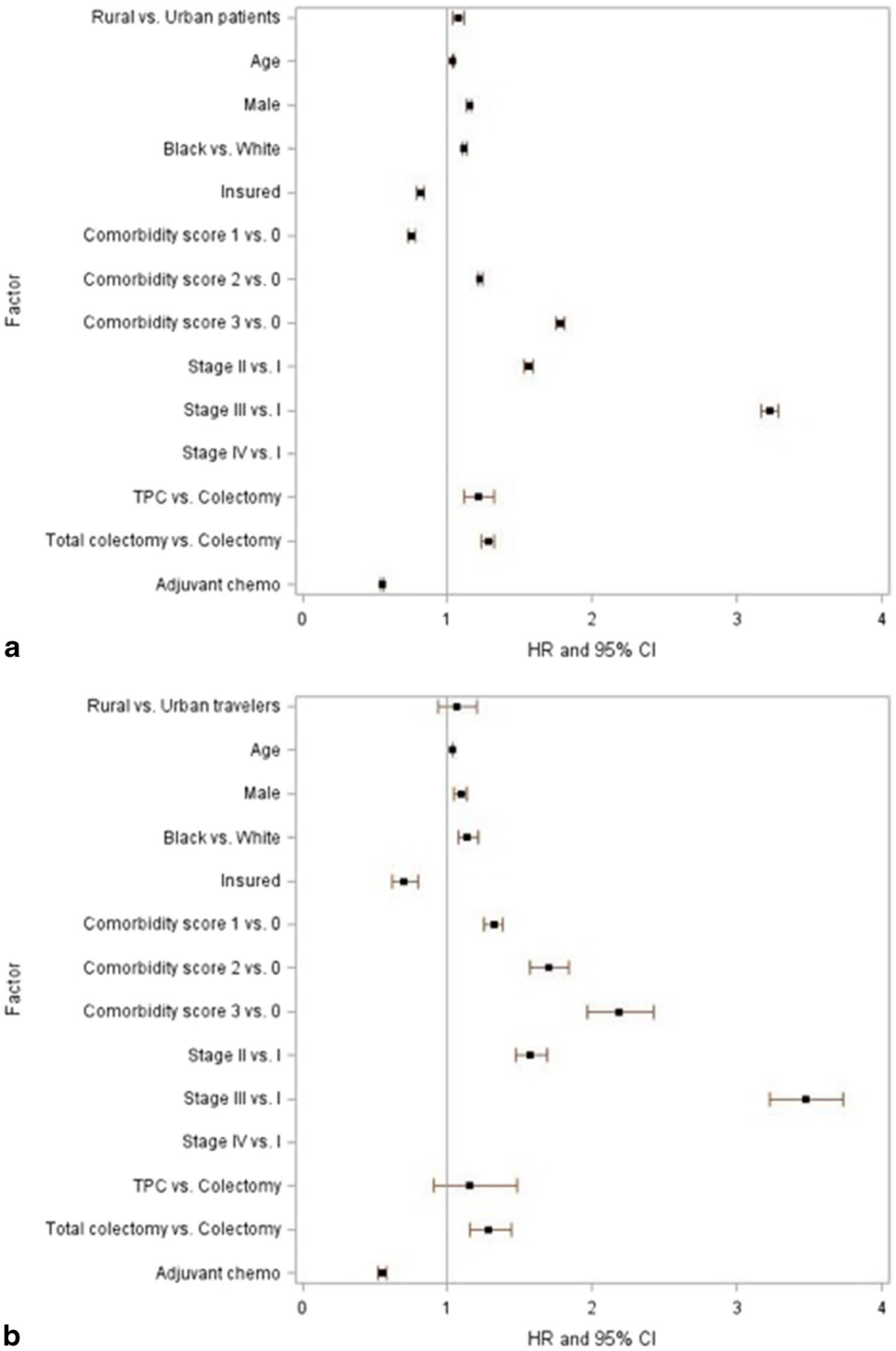

Fig. 2 Forest plots showing independent predictors of survival for **a** urban and rural patients with colon cancer and **b** urban and rural patients who traveled to a high-volume center for treatment

showed that 17% fewer rural patients undergo colon cancer screening compared to their urban counterparts.[18] Racial disparities compound the problem, with a large epidemiological analysis demonstrating that African Americans in rural areas had higher all- and colon cancer-related mortality compared to Caucasians in rural areas and African Americans in urban areas.[2] Rural patients have fewer resources for adequate cancer treatment. In our study, rural patients were less likely to have minimally invasive surgery and an adequate lymphadenectomy during surgery. The number of lymph nodes assessed during surgery correlates directly with survival for colon cancer and consequently the assessment of at least 12 lymph nodes has been accepted as a national consensus standard.[19–22]

Table 3 Background characteristics of rural and urban patients traveling to high-volume centers for treatment

	Rural ($N = 1276$)	Urban ($N = 46,781$)	p value
Patient age			< 0.0001
Median	70	68	
Q1, Q3	60.0, 78.0	57.0, 78.0	
Sex			0.2016
Male	663 (52.0%)	23,443 (50.1%)	
Female	613 (48.0%)	23,338 (49.9%)	
Race			< 0.0001
Black	74 (5.8%)	6680 (14.3%)	
White	1177 (92.2%)	38,090 (81.4%)	
Insurance type			< 0.0001
Medicare	795 (65.8%)	24,673 (54.3%)	
Private	327 (27.1%)	17,054 (37.5%)	
Medicaid	40 (3.3%)	1929 (4.2%)	
None	32 (2.6%)	1354 (3.0%)	
Charlson-Deyo score			0.0397
0	892 (69.9%)	32,617 (69.7%)	
1	252 (19.7%)	10,137 (21.7%)	
≥ 2	132 (10.3%)	4027 (8.6%)	
Hospital location			< 0.0001
South	627 (50.4%)	20,387 (45.0%)	
Midwest	571 (45.9%)	13,712 (30.3%)	
Northeast	27 (2.2%)	8424 (18.6%)	
West	20 (1.6%)	2774 (6.1%)	
Hospital type			< 0.0001
Academic	476 (38.2%)	25,339 (55.9%)	
Comprehensive	769 (61.8%)	19,958 (44.1%)	
Year of diagnosis			< 0.0001
2004	26 (2.0%)	1395 (3.0%)	
2005	51 (4.0%)	1986 (4.2%)	
2006	59 (4.6%)	2493 (5.3%)	
2007	78 (6.1%)	2983 (6.4%)	
2008	71 (5.6%)	3277 (7.0%)	
2009	91 (7.1%)	3657 (7.8%)	
2010	67 (5.3%)	3858 (8.2%)	
2011	115 (9.0%)	4323 (9.2%)	
2012	128 (10.0%)	4797 (10.3%)	
2013	179 (14.0%)	5524 (11.8%)	
2014	213 (16.7%)	5955 (12.7%)	
2015	198 (15.5%)	6533 (14.0%)	
Tumor size			0.0196
Median	44	41	
Q1, Q3	30.0, 60.0	28.0, 60.0	
High tumor grade	340 (28.8%)	9757 (23.2%)	< 0.0001
Metastatic disease at diagnosis			0.3064
No	1004 (78.9%)	36,287 (77.6%)	
Yes	269 (21.1%)	10,467 (22.4%)	
Clinical stage			0.0671
1	144 (27.7%)	6559 (31.7%)	
2	106 (20.4%)	3437 (16.6%)	

Table 3 (continued)

	Rural ($N = 1276$)	Urban ($N = 46,781$)	p value
3	66 (12.7%)	2494 (12.0%)	
4	203 (39.1%)	8227 (39.7%)	
Pathological stage			0.4302
1	254 (23.5%)	9408 (23.8%)	
2	315 (29.2%)	11,196 (28.3%)	
3	336 (31.1%)	11,830 (29.9%)	
4	174 (16.1%)	7092 (17.9%)	
Time to surgery (days)			0.0926
Median	19	20	
Q1, Q3	7.0, 34.0	8.0, 37.0	
Extent of surgery			0.1118
Segmental resection	963 (96.9%)	34,109 (95.7%)	
Total proctocolectomy	9 (0.9%)	308 (0.9%)	
Total colectomy	22 (2.2%)	1223 (3.4%)	
Minimally invasive technique			0.4892
No	312 (44.5%)	11,133 (45.8%)	
Yes	389 (55.5%)	13,154 (54.2%)	
Number of lymph nodes removed			0.9627
≥ 12	953 (87.6%)	34,366 (87.6%)	
< 12	135 (12.4%)	4843 (12.4%)	
Surgical margins			0.3307
Negative	1046 (94.8%)	37,493 (94.1%)	
Positive	57 (5.2%)	2351 (5.9%)	
Length of stay (days)			0.2618
Median	6	6	
Q1, Q3	4.0, 8.0	4.0, 8.0	
30-day readmission			0.3268
No	1180 (94.3%)	43,608 (94.9%)	
Yes	71 (5.7%)	2321 (5.1%)	
90-day mortality			0.0684
No	882 (93.2%)	33,027 (94.6%)	
Yes	64 (6.8%)	1878 (5.4%)	
Adjuvant chemotherapy			0.1
No	831 (70.3%)	29,027 (68.0%)	
Yes	351 (29.7%)	13,644 (32.0%)	

The survival disparity is mitigated when both rural and urban patients traveled to high-volume centers for treatment. Patients with colon cancer have improved mortality when undergoing surgery at a high-volume center,[4,5,23] with similar findings in other cancers.[4,24,25] A study in patients with rectal cancer undergoing abdominoperineal or low anterior resections revealed that non-colorectal surgeons and low-volume surgeons incur a higher local recurrence compared to colorectal surgeons and high-volume surgeons.[26] The volume-outcome relationship also translates to an economic benefit; the costs of cancer treatment at high-volume centers are lower than those incurred in low-volume centers.[6] These explanations likely account for the mitigation of survival difference between urban and rural patients who both travel to high-volume centers.

The access to high-volume treatment centers, however, may be an impediment in enabling rural patients and other disadvantaged groups to receive the best care. A retrospective analysis of ten complex operations in California found that non-Caucasians, uninsured patients, and patients on Medicaid were significantly less likely to go to high-volume centers, reinforcing the lack of access to such institutions.[27] A road network simulation study of Medicaid patients by Birkmeyer and colleagues estimated the time of transport to high-volume esophagectomy and Whipple centers and found that

rural patients had the longest travel time.[28] This travel time may be prohibitive for rural patients' caregivers who may have to miss work and incur personal and financial losses.[29] This lack of access likely explains the higher percentage of rural patients who remain unstaged with a cancer diagnosis.[8,9,30]

Our study has several limitations. It is a retrospective cohort analysis, and despite adjustment analyses has biases that are not controlled given the granularity of the NCDB. The NCDB also only records overall survival, rather than disease-free survival. This could confound survival analysis, but allows for comparison between other retrospective studies. Additionally, the definition of urban and rural populations is arbitrary in every study including ours, and these differences can confound findings. There was also a significant difference in the number of urban and rural patients in our study. The much smaller size of the rural population, and especially the size of the rural population that traveled to high-volume centers, limits our ability to generalize our findings. One of the major limitations is the effect size in our comparison of rural and urban patients. Compared to urban patients, rural patients had a worse baseline hazard of death of 6%, which was statistically significant, likely due to a high number of patients in the study, but not a sizeable difference. While our study found that travel to high-volume centers mitigated this statistically significant difference, the point estimate for the hazard ratio remained similar, which limits the external validity of the study. Finally, we used a national database with inherent limitations in recorded data, which in turn limits our understanding of staging, treatment decisions, and cancer-specific survival. For instance, we do not have information about referral patterns and patient decision making about seeking care at low vs. high volume centers.

Conclusions

This nationwide analysis reveals that rural patients with colon cancer have worse 5- and 10-year survival than urban patients. This survival difference is overcome by travel to a high-volume center for treatment, implying that access to quality cancer treatment centers can mitigate rural-urban disparities. Healthcare providers and policymakers should endeavor to build infrastructure to enable rural patients and other disadvantaged populations access to high-volume centers for cancer treatment.

Authors' Contributions Study design (MAA, MCT, JM); data acquisition (VR, MAA, MCT); interpretation (all authors); drafting manuscript (all authors); final approval (all authors); responsibility for the accuracy and integrity of the work (all authors).

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