

# Disparities in Characteristics, Access to Care, and Oncologic Outcomes in Young-Onset Colorectal Cancer at a Safety-Net Hospital

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**QUESTION ASKED:** Are there disparities in clinical characteristics and outcomes in patients with young-onset colorectal cancer in a safety-net setting?

**SUMMARY ANSWER:** In a cohort of 395 young-onset patients (49.6% Hispanic, 25.9% non-Hispanic Black, 20.0% non-Hispanic White, and 4.4% Others) diagnosed at a safety-net hospital in Dallas, Texas, non-Hispanic White race was independently associated with worse overall survival. Other factors independently associated with overall survival were having insurance, mismatch repair deficiency, and clinical stage.

**WHAT WE DID:** We performed a retrospective review of patients age < 50 years diagnosed and/or treated for colorectal cancer between 2001 and 2017 at a safety-net hospital in Dallas, TX. Kaplan-Meier and Cox regression models were constructed to compare overall survival, progression-free survival, and relapse-free survival by race and ethnicity, stratifying for relevant clinical and pathologic factors.

**WHAT WE FOUND:** Non-Hispanic White race was significantly associated with worse overall survival and

higher clinical stage, lack of insurance, and mismatch repair proficiency. Non-Hispanic Black patients were insured at higher rates than their Hispanic and non-Hispanic White counterparts, and non-Hispanic White patients also had a nonsignificant trend toward a higher rate of hospitalization during adjuvant therapy, but there was no difference between the groups regarding disruption in adjuvant.

**BIAS, CONFOUNDING FACTOR(S):** As with any retrospective chart abstraction study, there is a potential for selection bias given the necessity to exclude patients with complete data. Additionally, a safety-net population may not be generalizable to the United States.

**REAL-LIFE IMPLICATIONS:** This study provides valuable insight into clinical characteristics and outcomes of young-onset colorectal cancer in a safety-net population, which can help to improve access to quality cancer care for those facing the highest levels of healthcare disparities. The main conclusions of this study are that race and/or ethnicity, stage, insurance status, and mismatch repair status are significantly associated with survival outcomes.

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## abstract

**PURPOSE** Young-onset colorectal cancer is an emerging cause of significant morbidity and mortality globally. Despite this, limited data exist regarding clinical characteristics and outcomes, particularly in safety-net populations where access to care is limited. We aimed to study disparities in clinical characteristics and outcomes in patients with young-onset colorectal cancer in the safety-net setting.

**METHODS** We performed a retrospective review of patients < 50 years old diagnosed and/or treated for colorectal cancer between 2001 and 2017 at a safety-net hospital. Kaplan-Meier and Cox regression models were constructed to compare overall survival (OS), progression-free survival (PFS), and relapse-free survival (RFS) by race and ethnicity, stratifying for relevant clinical and pathologic factors.

**RESULTS** A total of 395 young-onset patients diagnosed at a safety-net hospital were identified and 270 were included in the analysis (49.6% Hispanic, 25.9% non-Hispanic Black, 20.0% non-Hispanic White, and 4.4% other). Non-Hispanic White race was independently associated with worse OS (hazard ratio [HR], 0.53; 95% CI, 0.29 to 0.97), as were lack of insurance, higher clinical stage, and mismatch repair proficiency. There was no significant difference seen in PFS or RFS between racial and ethnic groups.

**CONCLUSION** Non-Hispanic White race or ethnicity was found to be independently associated with worse OS in a safety-net population of patients with young-onset colorectal cancer. Other independent predictors of worse OS include higher stage, lack of insurance, and mismatch repair proficiency.

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## INTRODUCTION

Although incidence and mortality of colorectal cancer overall is decreasing,<sup>1</sup> the incidence of young-onset colorectal cancer has increased between 1% and 3% annually<sup>2,3</sup> and now accounts for 11% of colon cancer and 18% of rectal cancer cases in the United States.<sup>4</sup> This trend appears to be largely driven by an increase in rates of rectal cancer in the non-Hispanic White population.<sup>5</sup> Purported risk factors for young-onset colorectal cancer include obesity, family history of colorectal cancer, smoking, and inflammatory bowel disease.<sup>6-8</sup> Current screening guidelines, including the US Preventive Services Task Force,<sup>9</sup> generally recommend the initiation of a colorectal cancer screening program at the age of 50 years, whereas the American Cancer Society recently recommended initiation of screening at the age of 45 years for

average-risk patients.<sup>10</sup> Patients with young-onset colorectal cancer suffer from poor oncologic outcomes because of delayed diagnosis, increased symptom burden, higher stage at diagnosis, and lack of medical insurance.<sup>11</sup> It is estimated that there is a delay of 6 months from the onset of symptoms and diagnosis because of the low level of suspicion by the treating physicians.<sup>11</sup> These factors could disproportionately affect safety-net cohorts who have limited access to health care, as improved rates of insurance have been associated with improved access to guideline-compliant oncologic care, specifically rates of resection, and improvement in survival in colorectal cancer.<sup>12,13</sup> This may play a role both in diagnosis and management of young-onset colorectal cancer, particularly in vulnerable safety-net cohorts. There is a paucity of longitudinal clinical and pathologic data for this unique

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patient population in colorectal cancer within safety-net institutions. There is a need to better characterize the distinct clinical and molecular phenotypes of patients with young-onset colorectal cancer who present in this setting to improve risk stratification, influence treatment recommendations, and

improve outcomes. We therefore aimed to describe characteristics of patients with young-onset colorectal cancer presenting for treatment at a safety-net hospital, as well as identify racial and ethnic disparities in characteristics, treatment, and outcomes.

**TABLE 1.** Baseline Cohort Characteristics

Characteristic	NHB (n = 70)	Hispanic (n = 134)	NHW (n = 54)	P
Age (median)	46.0	42.0	44.0	<b>.018</b>
< 30	2 (2.9%)	13 (9.7%)	4 (7.4%)	
30-39	9 (12.9%)	38 (28.4%)	10 (18.5%)	
40-49	59 (84.3%)	83 (61.9%)	40 (74.1%)	
Sex (male)	35 (50.0%)	77 (57.5%)	36 (66.7%)	.177
Morphology				.640
Adenocarcinoma	68 (97.1%)	130 (97.0%)	54 (97.0%)	
Signet ring	2 (2.9%)	4 (3.0%)	0 (0.0%)	
Stage				.816
II	18 (25.7%)	36 (26.9%)	13 (24.1%)	
III	30 (42.9%)	65 (48.5%)	26 (48.1%)	
IV	22 (31.4%)	33 (24.6%)	15 (27.8%)	
Laterality				.230
Right	28 (40.0%)	43 (32.1%)	13 (24.1%)	
Left	42 (60.0%)	91 (67.9%)	41 (75.9%)	
Surgical resection				
II	17 (94.4%)	34 (94.4%)	12 (100%)	.248
III	29 (96.7%)	60 (92.3%)	26 (96.1%)	.102
IV	5 (22.7%)	6 (18.2%)	4 (25.0%)	.058
Received chemotherapy				
II	9 (50.0%)	18 (50.0%)	10 (76.9%)	.109
III	31 (96.9%)	63 (96.9%)	23 (88.5%)	.189
IV	18 (90.0%)	29 (87.9%)	10 (66.7%)	.062
CEA (median)	11.4	4.9	5.4	.130
Insured	44 (65.7%)	53 (40.5%)	26 (48.1%)	<b>.004</b>
Hospitalized	47 (79.7%)	99 (85.3%)	41 (91.1%)	.266
Days to surgery (median)	12.0	21.5	20.0	.589
Days to adjuvant (median)	57.0	50.0	58.5	.221
Positive margins	7 (13.7%)	13 (13.3%)	4 (11.8%)	.890
Lymphovascular invasion	21 (42.9%)	49 (52.1%)	16 (45.7%)	.542
Perineural invasion	10 (24.4%)	17 (20.5%)	10 (37.0%)	.221
LN sampled (median)	19.0	22.0	17.0	<b>.003</b>
Tumor deposits	10 (27.0%)	27 (35.5%)	8 (33.3%)	.664
Mismatch repair-deficient				
II	3 (18.8%)	13 (40.6%)	1 (11.1%)	.148
III	4 (16.0%)	14 (23.3%)	4 (21.1%)	.430
IV	0 (0.0%)	1 (3.7%)	1 (10.0%)	
KRAS-mutated	13 (37.1%)	33 (47.1%)	10 (43.5%)	.618

Abbreviations: LN, lymph nodes; NHB, non-Hispanic Black; NHW, non-Hispanic White.  
Bold indicates significant.

## METHODS

We performed a retrospective chart review on histologically confirmed patients with young-onset colorectal cancer, defined as < 50 years old at the time of diagnosis. Patients were diagnosed and/or treated at Parkland Health and Hospital System, a safety-net hospital in Dallas, Texas, between 2001 and 2017. This study was approved by the institutional review board at UT-Southwestern/Parkland. Patients with adenocarcinoma or signet-ring histology were included in the study. We included age at diagnosis, sex, race or ethnicity, insurance status, site of primary tumor, tumor laterality, stage, site of presentation, days to surgery, and adjuvant chemotherapy. We also collected information regarding disruption in adjuvant chemotherapy, preoperative CEA level, Eastern Cooperative Oncology Group performance status, molecular profile such as mismatch repair, and KRAS mutation status. Mismatch repair deficiency was defined as immunohistochemical staining showing lack of MLH1, MSH2, MSH6, or PMS2 expression. Insurance status was defined as having Medicare or Medicaid or private insurance at presentation. Financial coverage for evaluation and treatment provided by Parkland Health and Hospital System county system was considered as lack of insurance for the purpose of this study. This determination was made because this group of patients is without insurance and thus, without charity-based care, would have limited access to care. Right-sided tumors were defined from the cecum to (but not including) the splenic flexure, whereas left-sided was defined as distal to (and including) the splenic flexure, including rectum, based on previous studies.<sup>14</sup> Inpatient presentation was defined as index presentation in the emergency department or inpatient setting. Time to surgery was defined as the number of days from diagnosis via colonoscopy to colectomy. Time to adjuvant chemotherapy was defined as number of days from surgical resection to adjuvant chemotherapy (only stage II and III patients included, rectal cancer patients excluded). Adjuvant chemotherapy disruption was defined as dose-reduction or cessation of a chemotherapeutic agent, treatment delay (defined as > 1-week delay), or receiving < 6 months of adjuvant chemotherapy for any reason. Relapse-free survival (RFS) was calculated for stage II and III patients and was defined as the time from surgical resection to confirmed relapse. For stage IV patients, first-line progression-free survival (PFS) was defined as the time between start of first-line palliative treatment and progression of disease or death. Overall survival (OS) was defined as the time between diagnosis and death of any cause.

SPSS version 22 was used to conduct analyses to define clinical characteristics and investigate the potential influence of clinical variables on outcomes. Continuous and categorical variables were compared using a *t*-test,  $\chi^2$  test, or Fisher's exact test as appropriate. RFS, PFS, and OS were estimated by the Kaplan-Meier method. Differences in survival

outcomes were evaluated by the logrank test. Associations between variables and RFS, PFS, and OS were assessed by multivariable Cox proportional hazard regression analysis. Results were considered statistically significant if  $P < .05$ .

## RESULTS

### Baseline Characteristics

There were 395 patients with young-onset colorectal cancer diagnosed and/or treated during the study period. One hundred and twenty-five patients were excluded because of variable histology (14) and inability to verify dates of diagnosis, resection, or death (111), leaving 270 who had complete data and were included in analysis. The baseline characteristics of included patients are outlined in Table 1 and study design outlined in Figure 1. Fifty-seven percent were male and 42.6% were female, with a median age of 44.0 years (range, 19-49 years). Most patients were Hispanic (49.6%) followed by non-Hispanic Black (25.9%), and non-Hispanic White (20%). Hispanic patients were significantly younger than non-Hispanic Black and non-Hispanic White patients, with a median age of 42 years compared with 44 years and 46 years for non-Hispanic White and non-Hispanic Black, respectively ( $P = .011$ ). Seventy-two patients (26.7%) had stage II disease at presentation, whereas 127 patients (47.0%) and 71 patients (26.3%) had stage III and IV disease, respectively. Left-sided disease was more frequent (68.0%) but neither the stage at presentation nor laterality was significantly different between the ethnic and racial groups ( $P = .816$  and  $P = .230$ , respectively).

### Pathologic and Molecular Variables

Of the 224 patients with mismatch repair immunohistochemical staining data available, 43 (19.2%) of patients had mismatch repair deficiency and this status was

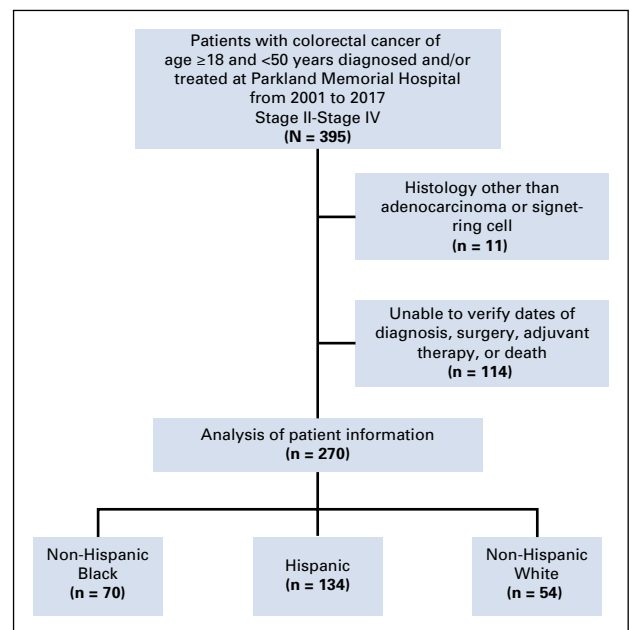


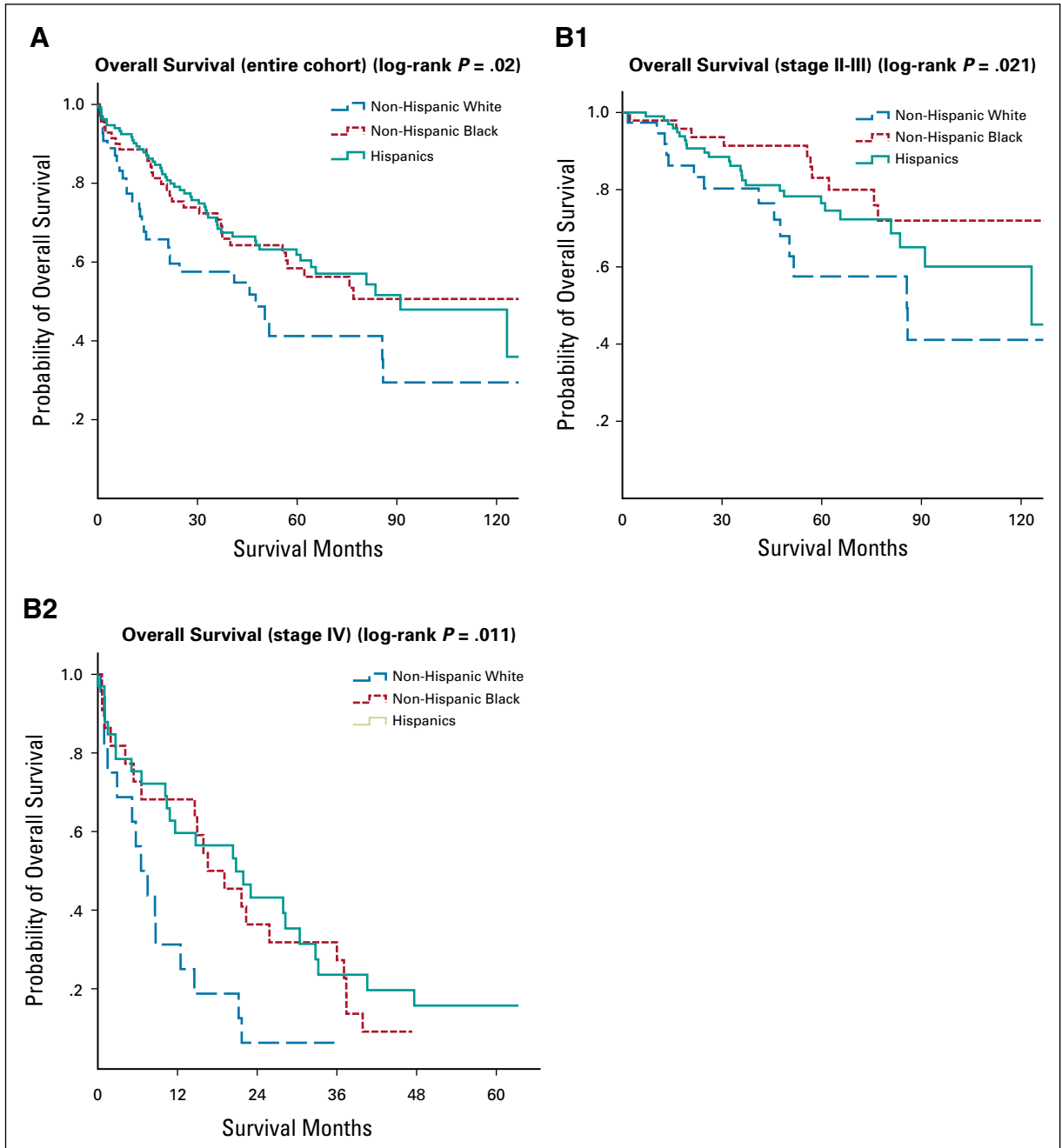
FIG 1. Study design.

significantly associated with stage at presentation ( $P < .001$ ), with more stage II disease presenting with mismatch repair deficiency compared with stage III and IV. KRAS mutational status data were available in 128 patients and 56 (43.8%) had KRAS mutations. Of the patients who underwent surgery of their primary tumor, 13.1% had positive margins, 47.5% had lymphovascular invasion, 24.8% had perineural invasion, and 31.9% had tumor deposits at the time of resection. The above-mentioned variables were without significant differences between the

groups. Hispanic patients had higher total number of lymph nodes resected at the time of surgery compared with other groups (median, 22, 19, and 17 for Hispanics, non-Hispanic Black, and non-Hispanic White, respectively;  $P = .003$ ).

**Healthcare Access or Treatment Variables**

One hundred thirty patients (49.4%) had insurance at the time of presentation. Non-Hispanic Black patients were more likely to be insured than Hispanic and non-Hispanic



**FIG 2.** (A) Overall survival (entire cohort) (logrank  $P = .02$ ). (B) Overall survival (stage II-III) (logrank  $P = .021$ ). Overall survival (stage IV) (logrank  $P = .011$ ).

White patients (65.7% v 40.5% v 48.1%, respectively;  $P = .0035$ ). Most patients (83.5%) presented to the hospital with symptoms and were diagnosed in the hospital admission without significant difference between groups ( $P = .266$ ). The median days to surgery from diagnosis and start of adjuvant chemotherapy from resection of primary tumor

(in stage II and III patients) were 20 days (range, 0-439 days) and 54.5 days (range, 15-336 days), respectively. There was no significant difference between rates of hospital presentation, days to surgery, or days to adjuvant chemotherapy between the groups. There was a trend in stage II non-Hispanic White patients receiving adjuvant chemotherapy at higher rates (76.9%) than Hispanic (50%) and non-Hispanic Black patients (50%) ( $P = .1092$ ). Non-Hispanic White patients also had a trend toward higher rate of hospitalization during adjuvant therapy (33.3% v 19.1% v 16.3%, respectively;  $P = .1095$ ). However, there was no difference between the groups regarding disruption in adjuvant therapy (68.3% non-Hispanic White, 62.1% Hispanic, and 67.3% non-Hispanic Black;  $P = .7282$ ). Non-Hispanic White patients with de novo metastatic disease tended to receive chemotherapy at lower rates than seen in Hispanic and non-Hispanic Black patients (66.7% v 90.0% v 87.7%, respectively;  $P = .0623$ ).

**TABLE 2.** Multivariable Analysis for Overall Survival

Characteristic	HR	95.0% CI		P
		Lower	Upper	
Race or ethnicity				
NHW	Ref			
NHB	0.541	0.301	0.971	<b>.040</b>
Hispanics	0.635	0.385	1.050	.077
Age				
< 30	Ref			
30-39	0.483	0.193	1.208	.120
40-49	0.740	0.320	1.711	.482
Sex				
Female	Ref			
Male	1.141	0.755	1.725	.531
Stage				
Stage II	Ref			
Stage III	1.757	0.900	3.431	.099
Stage IV	13.054	6.425	26.523	<b>&lt;.001</b>
Laterality				
Left	Ref			
Right	1.244	0.791	1.958	.345
Insurance				
Uninsured	Ref			
Insured	0.613	0.396	0.948	<b>.028</b>
Unknown	0.480	0.135	1.710	.258
ECOG				
ECOG 0	Ref			
ECOG 1	1.048	0.583	1.883	.876
ECOG 2+	1.856	0.768	4.486	.169
Unknown	1.388	0.773	2.493	.272
Mismatch repair				
Proficient	Ref			
Deficient	0.314	0.109	0.901	<b>.031</b>
Unknown	1.848	1.162	2.939	<b>.010</b>
KRAS status				
Wild-type	Ref			
Mutated	1.059	0.649	1.726	.819
Unknown	0.684	0.420	1.115	.127

Abbreviations: ECOG, Eastern European Oncology Group; HR, hazzard ratio; NHB, non-Hispanic Black; NHW, non-Hispanic White. Bold indicates significant.

### Survival Analysis

The 5-year survival rate for the entire cohort was 79.5% for stage II, 58.3% for stage III, and 5.0% for stage IV patients (Fig 2). The median OS for non-Hispanic Black patients was 134.5 months (95% CI, 56 to 126 months), whereas it was 91.1 months (95% CI, 34 to 234 months) for Hispanic and 47.5 months (95% CI, 17 to 77 months) for non-Hispanic White, respectively ( $P = .025$ ) (Table 3). In the multivariate analysis, non-Hispanic White race was independently associated with worse OS when stratified for age, sex, stage, laterality, insurance status, Eastern European Oncology Group performance status, and molecular profile (hazzard ratio [HR], 0.541; 95% CI, 0.301 to 0.971 for non-Hispanic Black patients; and HR, 0.635; 95% CI, 0.385 to 1.050 for Hispanic patients). Additional factors independently associated with survival were stage IV disease at presentation (HR, 13.05; 95% CI, 6.43 to 26.52), having insurance (HR, 0.613; 95% CI, 0.396 to 0.948), and mismatch repair deficiency (HR, 0.314; 95% CI, 0.109 to 0.901) (Table 2). Median RFS was 44.2 months and 37.0 months for stage II and III patients, respectively, with a median first-line PFS for metastatic patients of 7.4 months (Fig 3). For stage II and III patients, 5-year OS rates were 83% for non-Hispanic Black, 76% for Hispanic, and 57% non-Hispanic White patients ( $P = .021$ ). For stage IV patients, median OS was 20.4 months (95% CI, 10 to 32 months) for Hispanic, 17.8 months (95% CI, 9 to 24 months) for non-Hispanic Black, and 7.0 months (95% CI, 3 to 10 months) for non-Hispanic White ( $P = .011$ ) (Table 4).

### DISCUSSION

This study provides valuable insight into clinical characteristics and outcomes of young-onset colorectal cancer in a safety-net population, which can help to improve access to quality cancer care for those facing the highest levels of healthcare disparities. The main conclusions of this study are that race or ethnicity, stage, insurance status, and



**TABLE 3.** Univariable Analysis for OS, PFS, and RFS

Outcome	NHW	NHB	Hispanics	P			
				NHW*NHB	NHW*Hisp	NHB*Hisp	
Median OS, months	47	134	91	<b>.020</b>	<b>.028</b>	<b>.014</b>	.96
Median PFS, months	5	12	13	.25	.32	.11	.48
RFS (5-year rate)	52%	74%	62%	.23	.07	.31	.31

Abbreviations: NHB, non-Hispanic Black; NHW, non-Hispanic White; OS, overall survival; PFS, progression-free survival; RFS, Relapse-free survival.

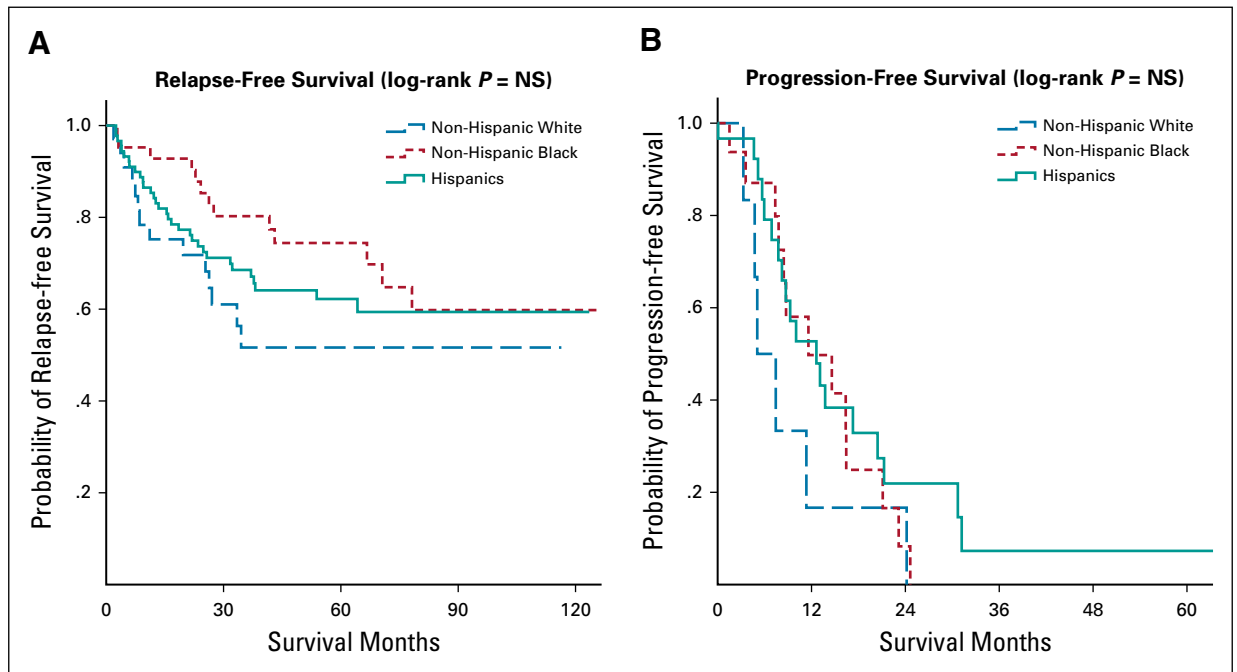
Bold indicates significant.

mismatch repair status are significantly associated with survival outcomes.

Non-Hispanic White race was found to be significantly associated with worse OS when controlling for other variables. This result was surprising, particularly given the fact that previously published data show that in a variety of young-onset malignancies including colorectal cancer, non-Hispanic Black patients tend to have poorer OS based on national databases, including the National Cancer Institute's SEER and National Cancer Database.<sup>19</sup> Thus, it is unclear whether this finding may be related to this specific safety-net population or whether this could be more generalizable. It is unknown whether ethnicity plays a role in aggressiveness of disease biology, varied response to treatment, or other pathologic or treatment-related factors. This question is important because of its implications in optimizing diagnostic and treatment algorithms for patients with young-onset colorectal cancer of diverse backgrounds and thus warrants further research. Non-Hispanic White patients did tend to receive chemotherapy at lower rates, particularly those who presented with stage IV disease

(90.0% for non-Hispanic Black, 87.9% for Hispanic, and 66.7% for non-Hispanic White;  $P = .062$ ). Although this did not reach statistical significance, this could represent differential goals or access to care within this study population, as there were also racial disparities in rates of insurance between racial and ethnic groups, with non-Hispanic Black patients having higher rates of insurance than non-Hispanic White and Hispanic patients. Other factors significantly associated with OS were stage at presentation and mismatch repair status, which have been reported previously.<sup>20</sup>

Despite the difficulties in comparing local data to that of national databases, this study found that the 5-year survival rates for patients with young-onset colorectal cancer were lower than those reported previously (79.5% for stage II, 58.3% for stage III, and 5.0% for stage IV patients in this cohort v approximately 90% for stage II, 70%-75% for stage III, and 20% for stage IV based on national studies<sup>4,21,22</sup>). There are multiple possible etiologies for this disparity. Safety-net hospitals are supported by taxpayers to provide health care to indigent populations who lack insurance because of socioeconomic factors or immigration status.



**FIG 3.** (A) Relapse-free survival (logrank  $P = NS$ ). (B) Progression-free survival (logrank  $P = NS$ ). NS, not significant.

**TABLE 4.** Univariable Analysis for OS Stratified by Stage of Disease

Outcome	NHW	NHB	Hispanics	P			
				NHW*NHB	NHW*Hisp	NHB*Hisp	
Stage II-III (5-year rate)	57%	83%	76%	<b>.021</b>	<b>.006</b>	.108	.212
Stage IV, median OS, months	7	17	21	<b>.011</b>	<b>.015</b>	<b>.008</b>	.528

Abbreviations: OS, overall survival; NHB, non-Hispanic Black; NHW, non-Hispanic White.

Bold indicates significant.

Approximately 50% of patients were insured within this cohort, so it is possible that the patients' worse OS may be because of decreased healthcare access, especially given the fact that insurance status was itself an independent predictor of OS in the multivariate analysis. Lack of insurance has a variety of downstream effects on patient outcomes. The patients in this study had a median of 54.5 days (range, 15-336 days) from surgical resection to adjuvant chemotherapy. Although there are no official guidelines regarding the optimal timing of adjuvant chemotherapy, > 8 weeks of delay has been associated with worse outcomes.<sup>23</sup> With the median time to adjuvant chemotherapy essentially right at 8 weeks in this study, this means that approximately 50% of these patients had a delay in care that could significantly affect oncologic outcomes. This delay could be related to a multitude of patients having their primary resection on an emergent basis at outside hospitals and needing to receive adjuvant chemotherapy at a safety-net institution because of lack of insurance. Regarding the disparity seen in those with de novo metastatic disease, it is possible that young patients presenting at a safety-net hospital who have limited access to care may present with worse metastatic disease burden, leading to a worse prognosis. Unfortunately, we could not study metastatic disease burden in this retrospective study. The patients in this study received similar rates of chemotherapy by stage to what has been published previously,<sup>21</sup> and thus, it is unlikely that undertreatment is to blame for the survival disparity.

Additionally, there was not a significant difference seen between groups receiving guideline-concordant therapies. Overall, this is further evidence of the need for Medicaid expansion in all states to improve access to quality and timely oncologic care, as expansion has been associated with improvements in early detection and survival in a variety of malignancies,<sup>24-26</sup> as well as decreasing disparities between racial and socioeconomic groups.<sup>27</sup>

As with any retrospective study reliant upon chart abstraction, there is potential for selection bias because of the necessity of excluding patients without data necessary for analysis. Also, while lack of comorbidity data is a limitation in the study, for the majority of patients in this safety-net setting, their index presentation with colorectal cancer was their first presentation to the medical system at large and given that our cohort of patients is young (< 50 years old), there is unlikely to be significant comorbidity affecting outcomes broadly within the cohort. Additionally, this is a cohort of patients diagnosed and treated at a safety-net hospital and thus, it may not represent the United States uniformly.

In conclusion, in a young-onset colorectal cancer population treated at a safety-net hospital, non-Hispanic White race or ethnicity was found to be independently associated with worse OS, and survival overall for the cohort was lower than that seen in national database studies. Other independent predictors of worse OS included higher stage, lack of insurance, and mismatch repair proficiency.

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## AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at DOI <https://doi.org/10.1200/OP.20.00777>.

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**Provision of study materials or patients:** Michael R. Folkert, Javier Salgado Pogacnik, Udit Verma, Amy Jones

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**Manuscript writing:** All authors

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**AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST****Disparities in Characteristics, Access to Care, and Oncologic Outcomes in Young-Onset Colorectal Cancer at a Safety-Net Hospital**

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