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Predictors of palliative treatment in stage IV colorectal cancer

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ABSTRACT

Background: Palliative treatment may be associated with prolonged survival and improved quality of life, but remains underutilized in stage IV colorectal (CRC). We examined a national cohort of stage IV CRC patients to determine the factors associated with palliative treatment.

Methods: Stage IV CRC patients, classified based on their survival length (<6 months, 6–24 months, and 24 + months), were analyzed using the American College of Surgeons National Cancer Data Base (2004–2013). Multivariable analysis was performed to evaluate factors associated with palliative treatment.

Results: Of 85,981 patients analyzed, 10.9% received palliative treatment. For 6–24 months survival, a more recent year of diagnosis, Medicaid, uninsured status, Mountain and Pacific regions were associated with higher odds of palliative treatment. For those who survived < 6 months, older patients had lower odds, while academic centers and residence > 20 miles from treating institutions were associated with increased likelihood of palliative treatment.

Conclusions: Palliative treatment in stage IV CRC is associated with a more recent year of diagnosis, Medicaid, academic centers, Mountain and Pacific regions of the US.

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Introduction

Recent studies suggest that approximately 20–30% of colorectal cancer (CRC) patients present with metastatic disease at diagnosis, and 40–65% of all CRC cases eventually progress to metastatic disease.^{1–4} Ultimately, approximately 80% of metastatic colorectal cancer (mCRC) cases are incurable,⁵ and thus palliative treatment becomes an important component of standard oncology care for these patients. Although previous studies have reported that palliative treatment for incurable cancer is associated with prolonged survival, decreased health care delivery costs, reduced utilization of hospital resources, and improved quality of life outcomes,^{6–10} it remains underutilized and understudied in stage IV colorectal. Early integration of palliative treatment is now considered the standard of care in the treatment of advanced

cancer,¹¹ thus underlying the need to address palliative treatment in stage IV CRC patients.

The modern approach to palliative treatment for incurable mCRC is multimodal, including any combination of surgery, multidrug chemotherapeutic regimens and radiation therapy. Currently, palliative surgery is the standard of care for most symptomatic mCRC patients, with obstruction, perforation, or bleeding.⁵ An expansion in the chemotherapeutic agents available in the last two decades has spurred an increased interest in the use of palliative chemotherapy in stage IV CRC.¹² Thus more palliative treatment options are now available to mCRC patients than in the past. The availability of palliative treatment options in a patient's clinical environment is no doubt an important determinant of palliative treatment utilization. However, even when palliative treatment is provided in patients' clinical environments, it is not yet fully understood why a significant proportion of patients who should receive palliative treatment do not. A few studies that have examined the sociodemographic and clinical factors associated with palliative treatment in gastrointestinal malignancies, reported

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that older age, female sex, African American race, and higher comorbidities are important determinants of palliative treatment utilization.^{13–15} However, an important missing piece from previous studies is contextualizing their findings in the settings of patient symptoms and need, and/or survival duration. Indeed, understanding the factors associated with palliative treatment receipt at various lengths of patient survival may help identify targeted interventions to increase the proper use of palliative treatment throughout the remainder of patient life.

In a previous study, we reported insurance status and geographic region as important determinants of palliative treatment among patients who die of CRC in the United States regardless of the clinical stage.¹⁶ However, stage IV CRC patients have a proportionally higher symptom burden and as a result may experience a higher need for palliative interventions, making this population unique in this regard. The present study examined a national cohort of stage IV CRC patients, who received treatment with palliative intent, to determine patient and hospital characteristics associated with the receipt of palliative treatment in stage IV CRC. We hypothesized that even when palliative treatment is provided in a patient's clinical environment, significant differences exist in palliative treatment receipt among stage IV CRC patients at varying survival durations.

Materials & methods

Patients and data source

The NCDB, a national cancer registry with more than 1500 accredited cancer programs, was the data source for this study. The NCDB captures >70% of newly diagnosed cancer cases in the United States, as well as data regarding surgical, chemotherapeutic/systemic, radiation and pain treatments provided strictly in a palliative manner. The dependent variable of interest was derived from the number of deceased patients in the 2016 NCDB with a diagnosis of Stage IV CRC during the years 2004 through 2013. Patients were stratified according to their length of survival from the disease (<6 months, 6–24 months, or >24 months) to provide a timing context. The rationale behind this was that short-surviving patients are more likely to have a more aggressive form of cancer in comparison to those who survived longer, thus providing an indicator of disease severity and need for palliative treatment in lieu of cancer-specific symptom burden which was not available in this dataset. The study was exempted from IRB review because of its use of de-identified publicly available dataset.

Outcome measures

Treatment information, outcomes, patient demographics, and information concerning treating facilities were included as covariates. Patient characteristics included age, year of diagnosis, sex,

race/ethnicity, primary insurance payer, median income, percentage with no high school diploma, urban or rural location, great circle distance from the treating institution, and Charlson–Deyo comorbidity score. Hospital characteristics included geographic region, facility type (academic versus nonacademic), and percentage of patients receiving palliative treatment. We calculated the percentage of patients receiving palliative treatment by using the number of CRC patients receiving palliative treatment at each hospital in the given year as the numerator and the total number of patients treated for CRC in the given year as the denominator. Patients receiving treatment in hospitals in which <0.5% CRC patients received palliative treatment were excluded from the study (n = 9, 221). We did this to ensure that palliative treatment was available at the hospitals included in the study. In addition, we only included patients receiving palliative treatment at the diagnosing center to better define care patterns and explore hospital characteristics associated with the provision of palliative treatment for CRC patients. Also excluded from the study were patients with stage 1, 2, 3 or unknown stage cancer (n = 192,721). In addition, cancer grade was included as a tumor-related variable. Palliative treatment was defined using NCDB palliative treatment variables/values which comprise treatments provided strictly with palliative intent.¹⁷ Values 1 through 7 were defined as palliative treatment received and 0 or 9 as no palliative treatment received (Table 1).

Statistical analysis

Data were described as percentages, and the Pearson χ^2 test was used to compare distributions of patient characteristics, hospital characteristics, and cancer grade across duration of survival. In addition, multivariable logistic regression models stratified by duration of survival were used to determine associations between palliative treatment and patient characteristics, hospital characteristics, and cancer grade. All tests of significance were 2-sided, $P < 0.05$ was considered significant, and analyses were performed using SAS version 9.4 (SAS Institute Inc).

Results

A total of 85,981 deceased patients with Stage IV CRC who only received treatment at diagnosing hospitals that provide palliative treatment options were identified; 10.9% received palliative treatment. The proportions of patients receiving palliative treatment decreased with increasing survival length (13.3%, 10.6%, and 6.8% for <6 months, 6–24 months, and >24 months survival respectively). Median ages at death were 68, 74, 65, and 62 years for overall, <6 months, 6–24 months, and >24 months survival groups respectively. The largest patient categories included female (50.6%), 50 years or older (88.2%), white (77.4%), Medicare insured (54%), Charlson–Deyo Comorbidity Score of 0 (70.7%), residence in metropolitan cities (83.5%), treating institutions located in East

Table 1
Definitions of NCDB palliative treatment variables.

| Value | Definition |
|-------|--|
| 0 | No palliative care provided, diagnosed at autopsy |
| 1 | Surgery (which may involve a bypass procedure) to alleviate symptoms, but no attempt to diagnose, stage, or treat the primary tumor is made |
| 2 | Radiation therapy to alleviate symptoms, but no attempt to diagnose, stage, or treat the primary tumor is made |
| 3 | Chemotherapy, hormone therapy, or other systemic drugs to alleviate symptoms, but no attempt to diagnose, stage, or treat the primary tumor is made |
| 4 | Patient received or was referred for pain management therapy with no other palliative care |
| 5 | Any combination of codes 1, 2, and/or 3 without code 4 |
| 6 | Any combination of codes 1, 2, and/or 3 with code 4 |
| 7 | Palliative care was performed or referred, but no information on the type of procedure is available in the patient record; palliative care was provided that does not fit the descriptions for codes 1–6 |
| 9 | It is unknown if palliative care was performed or referred; not stated in patient record |

Coast (44.8%) or Central (43.9%) regions, and treatment in nonacademic hospitals (70.3%) (Table 2).

Older patients who survived for < 6 months had lower odds of palliative treatment (odds ratio [OR], 0.92; 95% confidence interval [CI], 0.88–0.95). Meanwhile, patients who survived < 6 months and lived within 20–45 miles (OR, 1.26; 95% CI, 1.10–1.45) or > 45 miles

(OR, 1.24; 95% CI, 1.05–1.47) from the treating institution had higher odds of palliative treatment. For patients who survived between 6 and 24 months, Medicaid insurance (OR, 1.23; 95% CI, 1.06–1.44) and uninsured status (OR, 1.38; 95% CI, 1.16–1.65) were associated with higher odds of palliative treatment, while those with an unknown insurance status were less likely to receive palliative

Table 2
Patient demographics and clinical characteristics by duration of survival in patients with stage IV colorectal cancers.

| Characteristic | <6(n = 34,811) | 6-24(n = 33,106) | >24 (n = 18,064) | Total ^a (N = 85,981) | p-value |
|---|----------------|------------------|------------------|---------------------------------|---------------------|
| Survival, months | | | | | |
| Palliative Treatment | | | | | |
| Received palliative treatment | | | | | <0.001 ^b |
| Missing | 19 | 19 | 6 | 44 | |
| No | 86.7 | 89.4 | 93.2 | 89.1 | |
| Yes | 13.3 | 10.6 | 6.8 | 10.9 | |
| Type of palliative treatment | | | | | <.001 ^b |
| Missing | 19 | 19 | 6 | 44 | |
| None | 86.7 | 89.4 | 93.2 | 89.1 | |
| Surg/Rad/Chemo only | 8.1 | 9.2 | 6.2 | 8.1 | |
| Pain management only | 2.7 | 0.4 | 0.1 | 1.3 | |
| Both Surg/Rad/Chemo and pain management | 0.7 | 0.6 | 0.2 | 0.6 | |
| Unknown | 1.8 | 0.4 | 0.2 | 1.0 | |
| Patient Characteristics | | | | | |
| Age, y | | | | | <.001 ^b |
| <50 | 5.9 | 14.5 | 18.2 | 11.8 | |
| 50-64 | 21.4 | 33.5 | 40.3 | 30.0 | |
| 65-74 | 23.1 | 24.3 | 24.1 | 23.7 | |
| 75-84 | 31.2 | 20.7 | 14.5 | 23.6 | |
| ≥85 | 18.4 | 7.1 | 3.0 | 10.8 | |
| Age, Median (Q1, Q3) | 74 (63, 82) | 65 (55, 76) | 62 (53, 71) | 68 (57, 78) | <.001 ^c |
| Year of Diagnosis | | | | | <.001 ^b |
| 2004–2005 | 21.9 | 21.9 | 27.1 | 23.0 | |
| 2006–2007 | 21.1 | 22.3 | 28.2 | 23.1 | |
| 2008–2009 | 22.6 | 23.9 | 26.1 | 23.8 | |
| 2010–2011 | 23.3 | 22.4 | 16.5 | 21.5 | |
| 2012–2013 | 11.2 | 9.5 | 2.0 | 8.6 | |
| Sex | | | | | <.001 ^b |
| Female | 52.2 | 50.2 | 48.4 | 50.6 | |
| Male | 47.8 | 49.8 | 51.6 | 49.4 | |
| Race/Ethnicity | | | | | <.001 ^b |
| Missing | 94 | 119 | 52 | 265 | |
| White | 78.0 | 76.6 | 78.1 | 77.4 | |
| Black | 15.7 | 16.2 | 14.5 | 15.6 | |
| Hispanic | 3.4 | 3.8 | 4.0 | 3.6 | |
| Asian | 1.5 | 1.8 | 1.7 | 1.7 | |
| Other/Unknown | 1.4 | 1.7 | 1.7 | 1.6 | |
| Primary Payer | | | | | <.001 ^b |
| Private Insurance | 21.1 | 37.3 | 47.8 | 32.9 | |
| Medicaid | 5.4 | 7.0 | 6.0 | 6.1 | |
| Medicare | 66.8 | 48.7 | 39.2 | 54.0 | |
| Other Government | 0.7 | 0.9 | 0.9 | 0.8 | |
| Not Insured | 4.3 | 4.7 | 4.5 | 4.5 | |
| Insurance Status Unknown | 1.7 | 1.5 | 1.6 | 1.6 | |
| Median Income Quartiles (2008–2012) | | | | | <.001 ^b |
| Missing | 1052 | 1004 | 533 | 2589 | |
| <\$38,000 | 22.1 | 21.0 | 19.0 | 21.0 | |
| \$38,000-\$47,999 | 25.6 | 25.0 | 24.5 | 25.2 | |
| \$48,000-\$62,999 | 25.5 | 25.6 | 26.3 | 25.7 | |
| ≥\$63,000 | 26.7 | 28.4 | 30.1 | 28.1 | |
| Percentage with no High School Degree (2008–2012) | | | | | <.001 ^b |
| Missing | 1033 | 986 | 523 | 2542 | |
| ≥21 | 18.8 | 18.3 | 16.6 | 18.2 | |
| 13-20 | 28.2 | 27.3 | 27.3 | 27.7 | |
| 7.0–12.9 | 32.4 | 32.2 | 32.9 | 32.4 | |
| <7 | 20.6 | 22.2 | 23.1 | 21.7 | |
| Urban/Rural 2013 | | | | | 0.001 ^b |
| Missing | 1563 | 1483 | 826 | 3872 | |
| Metro > 1 million | 51.9 | 51.9 | 51.3 | 51.8 | |
| Metro 250 k to 1 million | 22.0 | 21.1 | 21.6 | 21.6 | |
| Metro fewer than 250 k | 10.2 | 10.0 | 10.3 | 10.1 | |
| Urban > 20 k adjacent to metro | 4.5 | 4.6 | 4.6 | 4.6 | |
| Urban > 20 k not adjacent to metro | 1.3 | 1.5 | 1.6 | 1.5 | |
| Urban 2.5 k to 19.9 k adjacent to metro | 5.4 | 5.9 | 5.8 | 5.7 | |

Table 2 (continued)

| Characteristic | <6(n = 34,811) | 6–24(n = 33,106) | >24 (n = 18,064) | Total ^a (N = 85,981) | p-value |
|---|----------------|------------------|------------------|---------------------------------|--------------------|
| Survival, months | | | | | |
| Urban 2.5 k to 19.9 k not adjacent to metro | 2.6 | 2.9 | 2.7 | 2.7 | |
| Rural/urban <2.5 k adjacent to metro | 1.0 | 0.9 | 1.0 | 1.0 | |
| Rural/urban <2.5 k not adjacent to metro | 1.1 | 1.2 | 0.9 | 1.1 | |
| Great Circle Distance, mi | | | | | <.001 ^b |
| Missing | 1014 | 967 | 510 | 2491 | |
| <2 | 14.5 | 11.7 | 10.8 | 12.6 | |
| 2–4 | 16.8 | 15.0 | 13.9 | 15.5 | |
| 4–9 | 27.8 | 26.3 | 25.3 | 26.7 | |
| 9–20 | 20.7 | 22.5 | 23.0 | 21.9 | |
| 20–45 | 11.9 | 14.0 | 15.4 | 13.5 | |
| >45 | 8.2 | 10.5 | 11.6 | 9.8 | |
| Charlson-Deyo Score | | | | | <.001 ^b |
| 0 | 64.1 | 74.4 | 76.9 | 70.7 | |
| 1 | 24.2 | 19.4 | 18.6 | 21.1 | |
| ≥2 | 11.8 | 6.2 | 4.5 | 8.1 | |
| Hospital Characteristics | | | | | |
| Geographic region | | | | | 0.08 ^b |
| Missing | 458 | 1231 | 824 | 2513 | |
| East Coast | 45.4 | 44.2 | 44.8 | 44.8 | |
| Central | 43.5 | 44.3 | 44.0 | 43.9 | |
| Mountain | 4.3 | 4.6 | 4.4 | 4.4 | |
| Pacific | 6.8 | 7.0 | 6.8 | 6.9 | |
| Facility Type | | | | | <.001 ^b |
| Missing | 500 | 1261 | 836 | 2597 | |
| Nonacademic Program | 73.4 | 68.8 | 66.7 | 70.3 | |
| Academic/Research program | 26.6 | 31.2 | 33.3 | 29.7 | |
| Percentage of CRC patients receiving PT | | | | | 0.002 ^b |
| 0.5–3 | 37.0 | 37.1 | 37.2 | 37.1 | |
| 3–6 | 41.6 | 42.6 | 42.5 | 42.2 | |
| >6 | 21.4 | 20.3 | 20.2 | 20.7 | |
| Tumor Characteristics | | | | | |
| Grade | | | | | <.001 ^b |
| Well differentiated | 3.4 | 4.5 | 6.6 | 4.5 | |
| Moderately differentiated | 31.8 | 46.6 | 59.7 | 43.4 | |
| Poorly differentiated | 26.3 | 25.8 | 18.1 | 24.4 | |
| Undifferentiated, anaplastic | 3.1 | 3.0 | 1.8 | 2.8 | |
| Cell type not determined | 35.4 | 20.1 | 13.8 | 25.0 | |

CRC – colorectal cancer PT – palliative treatment.

^a For missing data, values are number of patients; for other data, values are percentage of sample.

^b Chi-square.

^c Kruskal-Wallis.

treatment (OR, 0.60; 95% CI, 0.40–0.91). A median annual income of \$63,000 or more was also associated with higher odds of palliative treatment for patients who survived between 6 and 24 months (OR, 1.24; 95% CI, 1.05–1.46). A more recent year of diagnosis was associated with higher odds of palliative treatment for all durations of survival (OR, 1.15; 95% CI, 1.12–1.18 for < 6 months; OR, 1.18; 95% CI, 1.15–1.22 for 6–24 months; OR, 1.25; 95% CI, 1.18–1.32 for > 24 months). A higher tumor grade was associated with higher odds of palliative treatment compared to low grade tumors. There was no association between palliative treatment receipt and gender, race, education, or Charlson-Deyo Comorbidity Score (Table 3).

Patients who received treatment at academic hospitals had higher odds of palliative treatment if they survived <6 months (OR, 1.16; 95% CI, 1.07–1.25). The Mountain region was associated with higher odds of palliative treatment for those in the 6–24 months survival group (OR, 1.31; 95% CI, 1.07–1.61). Likewise, patients who received treatment in the Pacific region had higher odds of palliative treatment in the shorter surviving groups (OR, 1.50; 95% CI, 1.30–1.72 for < 6 months; OR, 1.23; 95% CI, 1.05–1.45 for 6–24 months). Residence in urban areas (population 2500–19 900) adjacent to a metropolitan city was associated with higher odds of palliative treatment among patients who survived 6–24 months (OR, 1.24; 95% CI, 1.03–1.49).

Discussion

The results of this study indicate that palliative treatment among patients with stage IV CRC remains low overall, with more palliative treatment usage occurring in shorter surviving patients. Our study demonstrates that palliative treatment in stage IV CRC is associated with younger patients, those diagnosed more recently, and those with Medicaid insurance or who were uninsured. Additionally, patients who received treatment in academic hospitals, resided in the Mountain and Pacific regions, or lived greater than 20 miles from the treating institution were more likely to receive palliative treatment. As hypothesized, the significance of these factors differs by survival duration. Ultimately, these findings advise that a tailored approach which addresses the unique characteristics of different patient subgroups should be favored by clinicians in efforts to optimize palliative treatment in stage IV CRC in the United States.

Despite the low palliative treatment usage in stage IV CRC, the longitudinal trend of palliative treatment utilization appears to be increasing, as greater use was observed among patients with a more recent year of diagnosis. It is important to emphasize this finding because it appears earlier calls focused at increasing the use of palliative treatment among stage IV CRC patients have been heeded. Other investigators have reported a similar progressive

Table 3
Multivariate associations between palliative treatment receipt and patient characteristics using logistic regression in deceased patients with stage IV colorectal cancers stratified by duration of survival.

| Covariate ^a | Odds Ratio (95% CI) | | |
|---|--------------------------------|--------------------------------|--------------------------------|
| | <6 months | 6–24 Months | >24 Months |
| Age | 0.92 (0.88, 0.95) ^d | 0.96 (0.92, 1.01) | 1.03 (0.95, 1.12) |
| Year of Diagnosis | 1.15 (1.12, 1.18) ^d | 1.18 (1.15, 1.22) ^d | 1.25 (1.18, 1.32) ^d |
| Male (ref Female) | 1.01 (0.94, 1.08) | 1.06 (0.98, 1.14) | 0.92 (0.81, 1.04) |
| Race/Ethnicity (ref White) | | | |
| Black | 0.99 (0.89, 1.09) | 1.09 (0.97, 1.22) | 1.09 (0.89, 1.33) |
| Hispanic | 1.21 (0.99, 1.47) | 1.14 (0.92, 1.41) | 1.17 (0.82, 1.66) |
| Asian | 0.98 (0.74, 1.28) | 1.11 (0.84, 1.48) | 0.81 (0.47, 1.38) |
| Other/Unknown | 0.80 (0.60, 1.08) | 1.03 (0.76, 1.40) | 0.66 (0.36, 1.19) |
| Primary Payer (ref Private) | | | |
| Medicaid | 0.97 (0.83, 1.14) | 1.23 (1.06, 1.44) ^c | 1.08 (0.83, 1.41) |
| Medicare | 0.96 (0.87, 1.06) | 1.10 (0.98, 1.22) | 0.87 (0.73, 1.04) |
| Other Government | 0.80 (0.53, 1.21) | 1.32 (0.88, 1.98) | 1.14 (0.58, 2.23) |
| Not Insured | 1.16 (0.98, 1.36) | 1.38 (1.16, 1.65) ^d | 0.97 (0.70, 1.32) |
| Insurance Status Unknown | 0.87 (0.65, 1.17) | 0.60 (0.40, 0.91) ^b | 0.77 (0.41, 1.44) |
| Median Income Quartiles 2008–2012 (ref <\$38 k) | | | |
| \$38,000–\$47,999 | 1.03 (0.93, 1.14) | 1.08 (0.96, 1.21) | 1.10 (0.90, 1.34) |
| \$48,000–\$62,999 | 1.06 (0.94, 1.18) | 1.11 (0.97, 1.27) | 1.00 (0.80, 1.25) |
| ≥ \$63,000 | 1.08 (0.94, 1.24) | 1.24 (1.05, 1.46) ^b | 1.03 (0.79, 1.35) |
| Percentage with no High School Degree (2008–2012) | 1.03 (0.98, 1.07) | 1.00 (0.94, 1.05) | 0.99 (0.91, 1.08) |
| Great Circle Distance (ref <2), mi | | | |
| 2–4 | 1.06 (0.93, 1.19) | 1.04 (0.89, 1.20) | 1.00 (0.78, 1.28) |
| 4–9 | 1.08 (0.97, 1.21) | 1.07 (0.93, 1.22) | 0.93 (0.74, 1.16) |
| 9–20 | 1.12 (1.00, 1.26) | 1.02 (0.89, 1.18) | 0.89 (0.71, 1.12) |
| 20–45 | 1.26 (1.10, 1.45) ^d | 1.01 (0.86, 1.19) | 0.94 (0.73, 1.21) |
| >45 | 1.24 (1.05, 1.47) ^b | 0.92 (0.76, 1.11) | 0.81 (0.60, 1.09) |
| Urban/Rural 2013 (ref Metro >1 million) | | | |
| Metro 250 k to 1 million | 0.95 (0.87, 1.04) | 1.03 (0.93, 1.14) | 1.08 (0.91, 1.28) |
| Metro fewer than 250 k | 0.93 (0.83, 1.05) | 1.05 (0.92, 1.20) | 1.09 (0.88, 1.35) |
| Urban > 20 k adjacent to metro | 0.99 (0.84, 1.17) | 1.08 (0.89, 1.30) | 1.23 (0.92, 1.64) |
| Urban > 20 k not adjacent to metro | 1.17 (0.89, 1.55) | 1.25 (0.93, 1.69) | 1.36 (0.84, 2.19) |
| Urban 2.5 k to 19.9 k adjacent to metro | 0.95 (0.80, 1.12) | 1.24 (1.03, 1.49) ^b | 1.10 (0.81, 1.49) |
| Urban 2.5 k to 19.9 k not adjacent to metro | 1.07 (0.86, 1.34) | 1.12 (0.88, 1.43) | 1.34 (0.91, 1.99) |
| Rural/urban <2.5 k adjacent to metro | 0.82 (0.58, 1.17) | 0.93 (0.61, 1.42) | 1.05 (0.57, 1.93) |
| Rural/urban <2.5 k not adjacent to metro | 0.93 (0.67, 1.28) | 1.47 (1.03, 2.09) ^b | 0.49 (0.19, 1.25) |
| Charlson–Deyo Score | 0.97 (0.93, 1.02) | 1.05 (0.98, 1.11) | 0.97 (0.87, 1.09) |
| Geographic region (ref East Coast) | | | |
| Central | 1.04 (0.97, 1.12) | 0.99 (0.92, 1.08) | 0.90 (0.79, 1.03) |
| Mountain | 1.17 (0.97, 1.42) | 1.31 (1.07, 1.61) ^c | 1.28 (0.91, 1.81) |
| Pacific | 1.50 (1.30, 1.72) ^d | 1.23 (1.05, 1.45) ^b | 1.11 (0.84, 1.48) |
| Academic Program (ref Nonacademic Program) | 1.16 (1.07, 1.25) ^d | 1.09 (1.00, 1.19) ^b | 0.97 (0.84, 1.12) |
| Percentage of CRC patients receiving PT | 2.47 (2.36, 2.59) ^d | 2.46 (2.33, 2.60) ^d | 2.73 (2.49, 3.00) ^d |
| Grade | 1.05 (1.03, 1.06) ^d | 1.07 (1.06, 1.08) ^d | 1.08 (1.05, 1.10) ^d |

^b P < 0.05; ^c P < 0.01; ^d P < 0.001.

CRC – colorectal cancer PT – palliative treatment.

^a The following were modeled ordinally: age categories (<50, 50–64, 65–74, 75–84, ≥85 years); year of diagnosis in 2–year categories (2004–2013); percentage with no high school diploma categories (≥21%, 13%–20%, 7%–12%, <7%); Charlson–Deyo score categories (0, 1, ≥2); grade categories for differentiation (well, moderately, or poorly, and undifferentiated). The logistic model included all covariates listed in the table.

trend in the utilization of palliative interventions for stage IV CRC in the last decade, and suggest this trend may be driven by progress in palliative chemotherapy.^{12,18} Conversely, reports on the trend of palliative radiation and surgery in stage IV CRC have been heterogeneous, though the use of palliative chemotherapy has been strongly correlated with the receipt of both.^{19,20} Remarkably, unlike previous studies, it is encouraging to find that no association was observed between palliative treatment receipt and gender, race or education, regardless of survival duration. Renouf et al. reported that the use of palliative chemotherapy was significantly associated with the male sex in patients with CRC.¹² Conversely, in a study of metastatic gastrointestinal tract cancers using the National Inpatient Sample, Okafor et al. demonstrated that females, African Americans, and Hispanics had significantly higher odds of inpatient palliative care.¹⁵ These traditional indicators of disparities in access to and utilization of health care services, including cancer care, have been the targets of numerous efforts to ensure equity of care in the past few decades.

While Kulaylat et al.¹³ found that age 60 years or older was significantly associated with a greater use of palliative interventions in stage IV rectal cancer, we found that age was only a significant predictor of palliative treatment among patients who survived less than 6 months. In this subgroup of patients (i.e. less than 6 months survival), younger patients had greater use of palliative treatment. However, it is important to note that the scope of the previous study was narrower, involving only rectal cancer patients. Additionally, unlike previous studies that have reported an association between a higher comorbidity burden and palliative treatment in metastatic rectal cancers,^{13,14} we observed no such association using the Charlson–Deyo comorbidity score as a measure of disease burden. We would expect the cancer-specific disease burden to be predictive of palliative treatment in mCRC due to the higher disease burden associated with advanced CRC. Unfortunately, the NCDB does not contain specific information on cancer-specific disease burden to conduct such an analysis.

Medicaid insurance has previously been associated with low

utilization of CRC testing and treatment and poorer outcomes in CRC.^{21–24} In contrast, we found that Medicaid insured or uninsured stage IV CRC patients who survived between 6 and 24 months had greater receipt of palliative treatment compared to commercial payers, yet the other time frames demonstrated no associations. We would expect a lack of insurance coverage to be associated with an increased risk of not receiving palliative treatment, presumably due to the costs of palliative interventions. However, the results suggest otherwise. It is possible that Medicaid insured and uninsured patients have delays in diagnosis, thus necessitating palliative intervention. But the absence of this association among those surviving less than 6 months raises the possibility of other mediating factors. It is also possible that a significant proportion of uninsured patients are wealthy people who can afford to pay the costs of palliative treatment, which may partly explain why this subgroup without insurance coverage often received palliative treatment. Further investigation is needed to elucidate this unusual association and clarify the mediators of palliative treatment among Medicaid and uninsured patients. Nonetheless, this finding may be encouraging as palliative treatment has been associated with decreased hospital costs at end of life^{25,26}; thus likely reducing the financial burden of cancer care on Medicaid and uninsured patients.

Several studies have reported geographic distance from treating facilities as a significant barrier to cancer services utilization.^{27–31} In contrast, we found that short surviving patients (i.e. less than 6 months) who lived greater than 20 miles from the treating institution were more likely to receive palliative treatment. Though this finding appears to depart from the current literature, Ambroggi et al. reported that increasing travel requirements from treating institutions are associated with more advanced disease at diagnosis, a worse prognosis, and a worse quality of life in cancer patients.³² Therefore, it is possible that stage IV CRC patients who need to travel long distances to receive cancer treatment, often present with late stages of metastatic disease or rapidly progressive disease, thus necessitating palliative treatment. This becomes a greater possibility when considering the longer surviving groups in which no association was seen between distance from treating institutions and palliative treatment. Moreover, though Okafor et al.¹⁵ reported that inpatient palliative treatment utilization was highest in urban teaching hospitals compared to rural hospitals among patients with GI cancers, we found that academic hospitals were associated with greater palliative treatment usage only in short surviving stage IV CRC patients. Academic hospitals are typically large urban hospitals, affiliated with medical schools and not-for-profit, all of which are institutional characteristics that have been associated with increased likelihood of having a specialized palliative care program.³³ Thus, it appears that even when specialized palliative care is offered in the patient's clinical environment, there may still be a preference for short-living patients regarding nonspecialized palliative treatment. We also found that stage IV CRC patients receiving treatment at hospitals in the Mountain (less than 6 months survival) and Pacific (less than 6 months and 6–24 months survival) regions were more likely to receive palliative treatment. This finding is similar to the results of the study conducted by Okafor et al.¹⁵ which reported that inpatient palliative treatment utilization was highest among GI cancer patients treated at hospitals in the West (Mountain and Pacific regions). This finding may be explained by differences in the overall pattern of palliative care utilization across various US regions. Dumanovsky et al.³³ reported that palliative care penetration was highest in the New England, Pacific, and Mid-Atlantic states and lowest in the West South Central and East South Central states. Though we did not observe significant differences in palliative treatment (among stage IV CRC patients) between the East Coast (New England and Mid-Atlantic) and Central regions in any of the

survival durations, our study demonstrates that the Pacific region continues to be associated with greater palliative treatment usage in patients surviving less than 24 months and a potential area of interest for future research to improve understanding of factors mediating increased palliative treatment utilization in the United States.

The strengths of our study include the use of a large national database which makes the findings generalizable, analysis of only hospitals that provide palliative interventions, and stratification of patients by survival duration to provide a timing context. This study is limited by the definitions of palliative treatment within the NCDB and the retrospective design. Within the NCDB, interventions designated as palliative are those provided in an effort to palliate or alleviate symptoms, but with non-curative intent. The NCDB does not differentiate between specialized palliative care, and interventions provided in a palliative manner by treating surgeons or physicians, but likely captures both modalities.¹³ Nonetheless, the NCDB data distinguishes between a treatment modality given for curative treatment from the same modality being used strictly for palliation. Caution is advised, however, when our study findings are interpreted in the setting of specialized palliative care. Furthermore, the NCDB lacks information regarding number of times, duration, and dates of palliative treatment. The NCDB also lacks specific information on the cancer-specific disease burden that the patient has, which would be more instructive than the duration of survival for palliative treatment. These missing information somewhat limit the ability to understand the nuances associated with the treatment and may overestimate or underestimate the influence of palliative treatment. The patients in the NCDB were identified from hospitals where they received a diagnosis or treatment and are not population-based (eg, the Surveillance, Epidemiology, and End Results registry). Finally, the retrospective nature of this data limits the ability to provide proactive suggestions concerning the appropriate interventions based on patient length of life. However, this analysis does provide greater context and evidence concerning similarities and differences associated with palliative treatment based upon patient length of life. Future clinical actions should focus on seeking to improve palliative treatment for stage IV CRC patients as early as reasonable and encouraging appropriate use throughout the remainder of the patient's life. In addition, studies should focus on articulating how duration and intensity of palliative treatment associate with patient outcomes and quality of life.

Conclusion

Our study indicates that palliative treatment in stage IV CRC is greater among more recently diagnosed patients, Medicaid and uninsured patients, academic centers, and Mountain and Pacific regions of the United States. The significance of these factors appears to differ by survival duration. Additional studies are needed to investigate factors mediating greater use of palliative treatment among Medicaid and uninsured patients, as well as in the Pacific region of the United States.

Disclosure

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