Association Between Primary Payer Status and Survival in Patients With Stage III Colon Cancer: An National Cancer Database Analysis

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Abstract

The goal of our study was to determine the between-insurance differences in survival in patients with pathologic stage III colon cancer using data from the National Cancer Database (NCDB). We identified 130,998 patients with pathologic stage III colon cancer in the NCDB diagnosed from 2004 to 2012. Patients with private insurance plans were 28%, 30%, and 16% less likely to die than were uninsured patients, Medicaid recipients, and Medicare beneficiaries, respectively.

Background: Colon cancer is the third most frequent cancer diagnosis, and primary payer status has been shown to be associated with treatment modalities and survival in cancer patients. The goal of our study was to determine the between-insurance differences in survival in patients with clinical stage III colon cancer using data from the National Cancer Database (NCDB). **Materials and Methods:** We identified 130,998 patients with clinical stage III colon cancer in the NCDB diagnosed from 2004 to 2012. Kaplan-Meier curves and multivariable Cox regression models were used to determine the association between insurance status and survival. **Results:** Patients with private insurance plans were 28%, 30%, and 16% less likely to die than were uninsured patients, Medicaid recipients, and Medicare beneficiaries, respectively. Medicare patients were 14% were less likely to die compared with uninsured patients. Patients receiving chemotherapy were, on average, 65% less likely to die compared with the patients not receiving chemotherapy. **Conclusion:** Private insurance and a greater socioeconomic status were associated with increased patient survival compared with other insurance plans or the lack of insurance. Future research should continue to unravel how socioeconomic status and insurance status contribute to the quality of care and survival of oncologic patients.

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Keywords: Colon cancer, Insurance status, National Cancer Database, Socioeconomic status, Survival outcomes

Introduction

Colon cancer is 1 of the leading causes of cancer-related deaths. Efforts such as increased screening practices have been made to reduce colon cancer-related deaths, which might have contributed to the decline in colon cancer incidence and death.[1] It has been estimated that 97,220 new colon cancer cases will be diagnosed, with 50,630 deaths, during 2018 in the United States.[2] These numbers place colon cancer as the fourth most common and second most deadly of all cancers. Many factors, such as staging and treatment, contribute to the colon cancer outcomes. One factor of increasing interest is the effect of health insurance on disease outcomes.

The discrepancy in survival when stratified by health insurance status in cancer has been demonstrated numerous times.[3-5] One study using the Surveillance, Epidemiology, and End Results database examined patients with a diagnosis of any of the top 10 deadliest cancers and found that Medicaid recipients and uninsured patients were more likely to die of their cancer than were those with non−Medicaid insurance (hazard ratio [HR], 1.44 and 1.47, respectively).[3] Another study examining multiple cancer types found that uninsured patients or those with Medicaid were more likely to present with late-stage cancer compared with privately insured patients (odds ratio, 2.0 and 1.6, respectively).[4] A study

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examining patients with stage I-III colon cancer in the United States found that those with private insurance had better 10-year survival probabilities compared with uninsured patients or those with public insurance (40.8% vs. 32.8%, respectively).[6]

Insurance status and its implications regarding accessibility to healthcare has been a major concern in politics. The Centers for Disease Control and Prevention found that 28.6 million people in the United States were uninsured in the first 9 months of 2016.[7] As the number of insured patients has increased, the benefits of differing insurance policies have been, and continue to be, evaluated.[8] Our study examined patients before the full effect of the Affordable Care Act, when more patients were uninsured. Since the time of our study, the Affordable Care Act expanded the eligibility for Medicaid and created healthcare markets to ease the process of purchasing insurance. The aim of the present study was to use the National Cancer Database (NCDB) to determine the association of survival and insurance type in patients with stage III colon cancer, a stage of colon cancer that allows for chemotherapy to be used as a quality measure.

Materials and Methods

The present retrospective cohort study used colon cancer hospital registry data collected from 2004 to 2012 within the NCDB. The NCDB is jointly sponsored by the Commission on Cancer of the American College of Surgeons and the American Cancer Society and includes ~70% of all newly diagnosed cases of cancer in the United States from > 1500 Commission-accredited cancer programs.[8] We were interested exclusively in patients with clinical stage III colon cancer. Stage III colon cancer was chosen to allow for chemotherapy to be used as a quality measure, because chemotherapy is widely considered standard treatment for stage III colon cancer.

Our primary outcome was overall patient survival, which was defined as the number of months from the date of diagnosis to their date of death, when they were lost to follow-up, or the date of study end (December 31, 2012). The NCDB does not collect cancer-specific survival. Our primary independent variable was a patient's insurance status. Specifically, we evaluated the survival differences among uninsured patients, patients with private insurance, and Medicaid recipients, Medicare beneficiaries, and an insurance plan sponsored by the US government (eg, Veterans Affairs, Public Health Service, Indian Health Service). The insurance status was defined according to what the patient was listed to have at the initial diagnosis and/or treatment. We also evaluated for survival differences in patient-level covariates, including age, race (white vs. not white), biologic sex, chemotherapy status (used or not used), comorbidities quantified by Charlson-Deyo score, and the population density, median income, and proportion of individuals who did not graduate high school in the zip code area in which the patients resided. Race was categorized as white and not white owing to the limited number of non-white patients with stage III colorectal cancer within each ethnic group; thus, we grouped the patients to allow for a more accurate analysis. Furthermore, we evaluated facility-level covariates, including the facility's structural characteristics (ie, community cancer program, comprehensive cancer program, academic/research cancer program, or other cancer program), population density (ie, metropolitan, urban, and rural), and the region of the United States in which the hospital was located as defined by the US Census Bureau (ie, Northeast, South, Midwest, and West).[9] Structural characteristics, as specified by the NCDB, depended on the program's number of new cancer cases annually and types of services provided. Community comprehensive cancer programs were those that saw ≥500 new cancer cases annually, and community cancer programs were those that 100 to 500 new cases annually. Academic centers were those that provided ≥500 new cases and postgraduate training in ≥4 categories, including internal medicine and general surgery.[10]

Statistical Analysis

Continuous variables are presented as the mean ± standard with between-insurance differences evaluated using the Kruskal-Wallis test with post hoc Mann-Whitney tests. Categorical variables are presented as frequencies and percentages, evaluated using the χ^2 tests with post hoc Fisher's exact tests. Unadjusted between-insurance differences in survival were evaluated using the Kaplan-Meier method with post hoc log-rank tests. All post hoc tests used the Bonferroni-adjusted $P < .008$ to indicate statistical significance. Multivariable Cox regression models were estimated to evaluate between-insurance differences in survival after adjusting for the listed patient- and facility-level covariates. The functional form for continuous covariates were evaluated using smoothed Martingale residuals. The proportionality of hazards assumption was evaluated graphically for each covariate using log-negative-log survival curves and statistically using interactions between the patient's insurance and time. Given the number of patients, clinically significant nonproportionality was suggested by interaction hazard ratios providing >1% moderation of the associated simple main effect (ie, interaction HR, < 0.99 to > 1.01). For all Cox regression models, a robust sandwich covariance matrix was used to account for the nesting of patients within facilities. This marginal Cox regression modeling approach was considered appropriate for the NCDB data (in lieu of a shared frailty or mixed-effects Cox regression models) given that these data represent a near population of newly diagnosed cancer cases. As such, all estimated HRs represent the populated-averaged effect across all patients and facilities. All statistical analyses were conducted using SAS, version 9.4 (SAS Institute, Cary, NC), with $P < .05$ used to indicate statistical significance when building the Cox regression model.

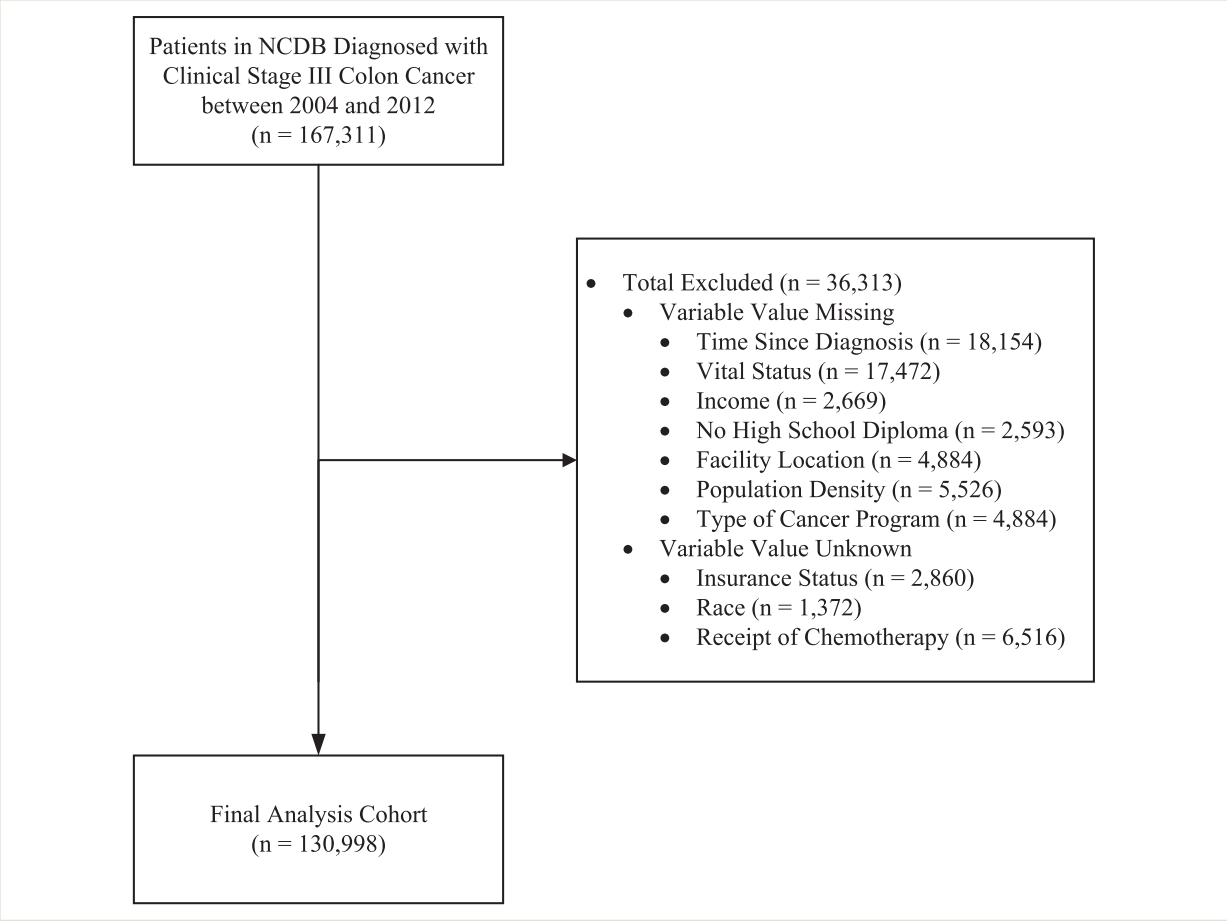
Results

Baseline Patient and Facility Characteristics

We initially identified 167,311 patients with clinical stage III colon cancer in the NCDB; however, given that Cox regression is a complete data technique, all baseline characteristics reported in the present study were based on the 130,998 patients with complete data for all patient- and facility-level covariates of interest. The patient exclusion data are shown in Figure 1. Of these patients, 3.3% were uninsured, 33.9% had private insurance, 4.1% were Medicaid recipients, 57.9% were Medicare beneficiaries, and 0.1% had another government-sponsored insurance policy.

The baseline patient and facility characteristics categorized by insurance status are listed in Table 1. Given the sample size, all omnibus comparisons were statistically significant, as were the overwhelming majority of post hoc comparisons. As expected, the

Figure 1 Flow Diagram Quantifying Patient Exclusion. The Total Number of Patients Excluded Does Not Equal the Number of Patients Summed Across All Missing or Unknown Variables Because the Patients Could Have Had Missing or Unknown Values for Multiple Variables



Abbreviation: NCDB = National Cancer Database.

Medicare beneficiaries were older, had the greatest rate of comorbidities, and had the greatest rate of death. These patients were a mean age of 75.9 ± 8.6 years, 10.9% had ≥ 2 comorbidities, and 53.5% died. Patients with private insurance plans generally lived in areas with greater socioeconomic status, received chemotherapy at the greatest rate, and had the lowest rate of death. Specifically, of those with private insurance, 34.8% lived in an area with a median income of ≥ $63,000, 25% lived in an area where < 7% of the population in that zip code did not have a high school degree, 82.9% received chemotherapy, and only 29.9% of these patients in our study died. The characteristics of uninsured patients and Medicaid recipients were similar except that uninsured patients were more likely to live in the South (55.7% vs. 36%, respectively) and Medicaid recipients were more likely to live in the Northeast (22.4% vs. 10.3%, respectively).

Unadjusted Survival Stratified by Insurance Status

The median length of follow-up was 35.7 months (interquartile range, 16.8-63.2 months) across all patients. The Kaplan-Meier survival curves stratified by insurance status are shown in Figure 2. The median survival time, indicating the exact time for which 50% of a specific insurance group had died, was 97.4 months (95% confidence interval [CI], 84.6-114.2 months) for uninsured patients, 125.4 months (95% CI, 123.4-128.9 months) for patients with private insurance, 75.3 months (95% CI, 70.6-82.1 months) for Medicaid recipients, 49.0 months (95% CI, 48.3-49.8 months) for Medicare beneficiaries, and 91.4 months (95% CI, undefined) for patients with another government-sponsored insurance plan. The results of the omnibus log-rank test were statistically significant ($\chi^2_4 = 7207.0$; $P < .001$). Statistically significant differences in survival time were indicated between all insurance status groups ($P < .001$), except for between Medicaid recipients and patients with another government-sponsored insurance plan ($P = .394$).

Adjusted Survival Stratified by Insurance Status

Before estimating the multivariable Cox regression model, smoothed Martingale residuals suggested an overadditive quadratic effect for patient age at diagnosis, indicating that the increased risk

Table 1 Descriptive Statistics for Demographic and Clinical Variables Stratified by Primary Payer

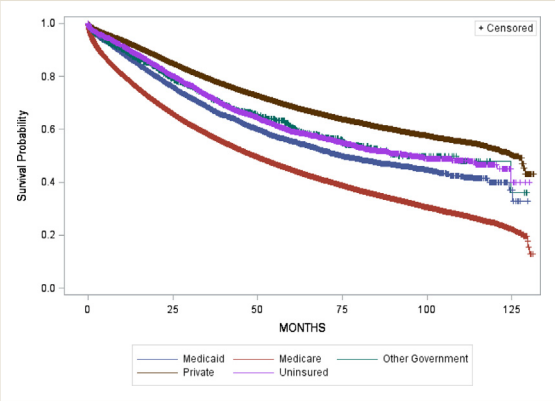
Variable	Uninsured Patients (n = 4378)	Private Insurance (n = 44,466)	Medicaid Recipients (n = 5370)	Medicare Beneficiaries (n = 75,850)	Other Government (n = 934)	*P* Value
Follow-up, mo	41.0 ± 29.4	49.6 ± 31.7	40.0 ± 29.3	38.0 ± 30.9	41.7 ± 30.3	<.001
Age, y	56.5 ± 8.8	59.0 ± 10.6	58.5 ± 10.5	75.9 ± 8.6	62.7 ± 11.8	<.001
White race	68.1	82.4	64.3	87.2	75.3	<.001
Female gender	48.4	48.9	52.1	55.2	42.2	<.001
Chemotherapy	78.9	82.9	74.0	55.3	75.8	<.001
Charlson-Deyo comorbidity score						<.001
0	79.6	78.4	70.8	63.0	72.3	
1	16.6	17.5	21.0	26.1	20.3	
2	3.9	4.0	8.2	10.9	7.4	
Median household income						<.001
<$38,000	30.5	16.1	32.6	18.9	20.8	
$38,000-$47,999	27.8	21.9	26.2	25.2	27.1	
$48,000-$62,999	23.3	27.2	23.9	26.9	28.9	
≥$63,000	18.5	34.8	17.3	29.0	23.2	
No high school diploma						<.001
≥ 21%	32.4	16.5	33.0	16.8	16.9	
13%-20.9%	31.8	25.2	30.9	26.7	28.6	
7%-12.9%	23.2	33.3	25.6	33.9	36.0	
<7%	12.7	25.0	10.5	22.6	18.5	
Population density						<.001
Metropolitan	84.1	87.0	86.2	82.6	80.6	
Urban	14.1	11.5	12.1	15.0	16.4	
Rural	1.8	1.4	1.7	2.3	3.0	
Facility type						<.001
Community	13.8	12.9	15.4	16.2	16.1	
Comprehensive	41.8	51.8	38.6	53.9	54.0	
Academic/research	36.0	27.6	37.6	22.5	21.8	
Other	8.5	7.7	8.4	7.5	8.1	
Facility region						<.001
Northeast	10.3	20.2	22.4	19.9	7.2	
South	55.7	37.6	36.0	36.3	55.7	
Midwest	19.7	24.9	22.4	29.7	18.1	
West	14.3	17.3	19.2	14.1	19.1	
Died	33.8	29.9	38.9	53.5	34.2	<.001

Data presented as percentages, unless otherwise noted.

of death due to age at diagnosis was significantly larger for patients who were older at diagnosis. Furthermore, a violation of the proportionality of hazards assumption was indicated for chemotherapy status, which was addressed by including the interaction between chemotherapy status and linear time (the interaction with quadratic time was not statistically significant). No proportionality violation was observed for any other covariate, indicating that estimated HRs for the remaining covariates were constant throughout the entire follow-up period.

The adjusted HRs for all variables included in the final multivariable Cox regression model (Table 2). Insurance status was a statistically significant predictor of survival after adjusting for age, race, biologic sex, chemotherapy status, comorbidity score, income, education, population density, facility type, and region of the United States ($\chi^2_4 = 320.0$; $P < .001$). Specifically, patients with private insurance had an average 27.8% (95% CI, 23.2%-32.2%), 29.9% (95% CI, 26.1%-33.5%), and 16.0% (95% CI, 13.6%-18.3%) lower risk of death relative to uninsured patients, Medicaid recipients, and Medicare beneficiaries, respectively. Although patients with private insurance also had an average 11.3% (95% CI, 0.0%-21.4%) lower risk of death compared with patients with another government-sponsored insurance plan, this result was not

Figure 2 Kaplan-Meier Survival Curves Stratified by Insurance Status Group



statistically significant. In addition, patients with another government-sponsored insurance plan had an average 18.6% (95% CI, 7.0%-28.8%) and 21.0% (95% CI, 9.8%-30.8%) lower risk of death relative to uninsured patients and Medicaid recipients, respectively. In contrast, Medicare beneficiaries had an average 16.5% (95% CI, 11.8%-21.0%) lower risk of death relative to Medicaid recipients. Medicare patients had an average 14.1% (95% CI, 8.4%-19.4%) lower risk of death compared with uninsured patients. Finally, no adjusted survival differences were observed between uninsured patients and Medicaid recipients nor between patients with another government-sponsored insurance plan and Medicare beneficiaries.

Regarding the patient- and facility-level covariates, the instantaneous risk of dying was significantly greater for patients who were older at diagnosis, which was expected (ie, relative to patients aged 40 years, 1% increase in risk for a patient aged 50 years at diagnosis, and a 4% increase in risk for a patient aged 80 years at diagnosis). Furthermore, patients with more comorbidities and patients living in zip codes with lower socioeconomic status had a greater risk of death. In contrast, patients being treated in the West or at an academic medical center had a lower risk of death. No differences were indicated by population density. Overall, of all the variables examined, the risk of death, on average, was greatest for those who did not receive chemotherapy compared with those who received chemotherapy. Patients with private insurance received a greater percentage of chemotherapy than did uninsured patients (82.9% and 78.9%, respectively). Medicaid and Medicare patients had the lowest receipt of chemotherapy (74.0% and 53%, respectively). The effect of chemotherapy changed over time such that at 6, 12, and 18 months after diagnosis, the risk of dying without chemotherapy changed over time (HR, 0.32, 0.35, and 0.39, respectively).

Discussion

Our results showed that patients with private insurance averaged the greatest probability of survival compared with other primary payer groups, a result consistent with previous studies evaluating primary payer status in other cancers.[11-13] One such study examined 7445 patients with colorectal cancer and found that patients with private insurance had a 29% and 36% decreased risk of death compared with uninsured patients and Medicaid recipients, respectively.[14] These results were supported almost identically by our considerably larger study.

We also found that the receipt of chemotherapy had the largest association with survival, and that private insurance patients received chemotherapy at the greatest rate compared with other insurance types. Differences in perception of the differing insurance policies by doctors could affect treatment. Studies have shown that doctors' hesitate in accepting Medicaid patients owing to the decreased Medicaid payment.[15] In our study, patients with Medicare or Medicaid had the lowest rates of chemotherapy (55.3% and 74%, respectively).

Although the effect of chemotherapy diminished slightly as the time from the diagnosis increased (regardless of primary payer), patients receiving chemotherapy averaged an ~65% greater likelihood of survival across the entire follow-up length, a finding that aligns with those from previous studies.[16,17] Furthermore, we found that only 55.3% of Medicare patients received chemotherapy. Although this was consistent with the rates indicated in previous studies,[17,18] this low rate is concerning given that studies have shown the benefit of chemotherapy in elderly patients.[19,20] For example, a study using the Surveillance, Epidemiology, and End Results database found that those aged >75 years had an increased chance of survival if given chemotherapy (HR, 0.60; 95% CI, 0.53-0.68).[21]

We found no survival differences between uninsured patients and Medicaid recipients. These groups were very similar, with a < 2% difference in education, population density, income, and institution type. However, uninsured patients had fewer comorbidities (79.6% and 70.8%, respectively) and received chemotherapy at a greater rate compared with Medicaid recipients (78.9% and 74.0%, respectively). Although our data suggest that uninsured patients receive care that is, at a minimum, comparable to that of Medicaid recipients, we acknowledge that the uninsured patients in our study might not reflect the national uninsured population. Our reasoning is based on that the NCDB only includes newly diagnosed cancer patients from American College of Surgeons (ACS) hospitals, which have been shown to be located in urban settings more often than non-ACS hospitals.[22] Because the Centers for Disease Control and Prevention has estimated that ~19.3% of the US population live in rural areas[23] and rural patients are more likely to be uninsured and more likely to die of their cancer,[24,25] our study likely missed a significant proportion of rural patients, which could have resulted in an overestimation of survival in the uninsured.

The limitations of our study included that the NCDB only reports all-cause mortality; therefore, the exact colon cancer-related mortality rate is unknown. This lack of classification could have affected our survival estimates, especially for older patients with Medicare. Most patients in the present study were classified as white, and the nonwhite subgroups had significantly fewer patients within each race. To ensure proper analysis, the nonwhite patients were grouped together. Although improving the analysis, this grouping limited our ability to gain greater insight regarding the other races in the study. The present study was also limited to the years for which the patient data were available. The Affordable Care

Table 2 Results of Final Marginal Multivariable Cox Regression Model

Variable	HR	95% CI for HR	*P* Value
Age at diagnosis, y			
50	1.01	1.01-1.01	<.001
65	1.02	1.02-1.02	<.001
80	1.04	1.03-1.04	<.001
White versus not white	0.99	0.96-1.02	.479
Female versus male	0.85	0.84-0.87	<.001
Chemotherapy versus no chemotherapy			
6 mo after diagnosis	0.32	0.31-0.33	<.001
12 mo after diagnosis	0.35	0.34-0.36	<.001
18 mo after diagnosis	0.39	0.38-0.40	<.001
Charlson-Deyo comorbidity score			
0	0.65	0.63-0.66	<.001
1	0.77	0.74-0.79	<.001
2	Reference		
Median household income			
<$38,000	1.11	1.07-1.15	<.001
$38,000-$47,999	1.06	1.03-1.10	<.001
$48,000-$62,999	1.04	1.01-1.07	.007
≥$63,000	Reference		
No high school diploma			
≥21%	1.08	1.03-1.12	<.001
13%-20.9%	1.09	1.05-1.12	<.001
7%-12.9%	1.06	1.03-1.09	<.001
<7%	Reference		
Population density			
Metropolitan	1.01	0.95-1.07	.770
Urban	1.03	0.97-1.10	.370
Rural	Reference		
Facility type			
Community	1.03	0.99-1.09	.183
Comprehensive	0.99	0.95-1.04	.776
Academic/research	0.94	0.89-0.99	.016
Other	Reference		
Facility region			
Northeast	1.06	1.02-1.11	.006
South	1.05	1.01-1.08	.019
Midwest	1.06	1.02-1.10	.003
West	Reference		
Primary payer			
Private versus uninsured	0.72	0.68-0.77	<.001
Private versus Medicaid	0.70	0.67-0.74	<.001
Private versus Medicare	0.84	0.72-0.86	<.001
Private versus other government	0.89	0.79-1.00	.052
Medicaid versus uninsured	1.03	0.96-1.11	.436
Medicare versus uninsured	0.86	0.81-0.92	<.001
Other government versus uninsured	0.81	0.71-0.93	.003
Medicare versus Medicaid	0.84	0.79-0.88	<.001
Other government versus Medicaid	0.79	0.69-0.90	<.001
Medicare versus other government	1.06	0.94-1.19	.376

The reference group for covariates with ≥ 3 categories is indicated; the reference group for all 2-category comparisons is noted by "versus" For example, the adjusted HR of 0.72 for private versus uninsured indicates that patients with private insurance had an average ~28% lower risk of death relative to uninsured patients (ie, [1 − 0.72] × 100 = 28%).
Abbreviations: CI = confidence interval; HR = hazard ratio.

Act was in full effect after the study period; thus, the demographic data of the patients within the insurance types has likely changed. We also did not have access to data regarding the prevalence of other lifestyle factors, such as smoking habits. It has been shown that smokers have a 23% greater likelihood of developing colon cancer compared with nonsmokers.[26] However, the Charlson-Deyo score includes chronic pulmonary disease, which likely accounted for smoking habits to some degree. The inability to fully encompass the demographic differences among the insurance groups also limited our ability to fully comprehend the sole effect of insurance status on survival. Although many variables were controlled for, correlation should not be mistaken for causation in our report. Finally, the NCDB does not included data for the ~30% of patients with newly diagnosed cancer that was diagnosed outside of ACS hospitals; thus, it is unknown whether these missing patients differed significantly from the patients in our study. However, despite our inability to access those 30% of patients, the NCDB serves as an invaluable resource that allowed us to examine 70% of patients with newly diagnosed cancer.

Conclusion

The present study examined significant differences in colon cancer survival between primary payer groups after adjusting for relevant patient- and facility-level characteristics. Clear demographic differences were found among the patients with different insurance types, with patients with private insurance consistently having the best outcomes. Medicaid and uninsured patients were comparable in their risk of death. Despite the number of patients with insurance increasing over time, many patients remain poorly insured and are at an increased risk of death.

Clinical Practice Points

- The discrepancy in survival according to health insurance status in cancer has been demonstrated numerous times.
- The goal of the present study was to address potential discrepancies in survival outcome among patients with stage III colon cancer with different insurance types.

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