Medicare/Medicaid Insurance, Rurality, and Black Race Associated With Provision of Hepatocellular Carcinoma Treatment and Survival

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ABSTRACT

Background: Early treatment of hepatocellular carcinoma (HCC) is associated with improved survival, but many patients with HCC do not receive therapy. We aimed to examine factors associated with HCC treatment and survival among incident patients with HCC in a statewide cancer registry. **Materials and Methods:** All patients with HCC from 2003 through 2013 were identified in the North Carolina cancer registry. These patients were linked to insurance claims from Medicare, Medicaid, and large private insurers in North Carolina. Associations between prespecified covariates and more advanced HCC stage at diagnosis (ie, multifocal cancer), care at a liver transplant center, and provision of HCC treatment were examined using multivariate logistic regression. A Cox proportional hazards model was developed to assess the association between these factors and survival. **Results:** Of 1,809 patients with HCC, 53% were seen at a transplant center <90 days from diagnosis, with lower odds among those who were Black (adjusted odds ratio [aOR], 0.54; 95% CI, 0.39–0.74), had Medicare insurance (aOR, 0.35; 95% CI, 0.21–0.59), had Medicaid insurance (aOR, 0.46; 95% CI, 0.28–0.77), and lived in a rural area; odds of transplant center visits were higher among those who had prediagnosis alpha fetoprotein screening (aOR, 1.74; 95% CI, 1.35–2.23) and PCP and gastroenterology care (aOR, 1.66; 95% CI, 1.27–2.18). Treatment was more likely among patients who had prediagnosis gastroenterology care (aOR, 1.68; 95% CI, 0.98–2.86) and transplant center visits (aOR, 2.42; 95% CI, 1.74–3.36). Survival was strongly associated with age, cancer stage, cirrhosis complications, and receipt of HCC treatment. Individuals with Medicare (adjusted hazard ratio [aHR], 1.58; 95% CI, 1.20–2.09) and Medicaid insurance (aHR, 1.55; 95% CI, 1.17–2.05) had shorter survival than those with private insurance. **Conclusions:** In this population-based cohort of patients with HCC, Medicare/Medicaid insurance, rural residence, and Black race were associated with lower provision of HCC treatment and poorer survival. Efforts should be made to improve access to care for these vulnerable populations.

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Background

Hepatocellular carcinoma (HCC) incidence and mortality are increasing in the United States.^{1,2} The prognosis for HCC is poor, in part because potentially curative treatments, including surgical resection, ablation, and transplantation, are feasible in just a minority of patients with early-stage HCC.³ In the absence of curative therapy, liver-directed locoregional therapies and drug therapy prolong survival, yet up to half of all patients with HCC never receive any cancer-directed therapy.^{4–7}

Despite accumulating evidence that the provision of timely HCC treatment decreases cancer-related mortality,⁸ treatment rates remain low and the reasons for nonreceipt of therapy in patients with HCC remain unclear. Medical comorbidities, decompensated liver disease, and advanced HCC often preclude specific HCC-directed therapies. Other potential factors have been associated with the low provision of HCC therapy, including older patient age, insurance status, and care at a low-volume center.^{9–11} In addition, racial and ethnic disparities in the receipt of HCC treatment and survival have been well-documented.^{12–16} Finally, subspecialist consultation has been associated with improved treatment outcomes in the US Department of Veterans Affairs system.¹⁷ This evidence suggests that both patient- and facility-level factors likely influence the provision of HCC treatment. However, relatively few data sources allow for the simultaneous investigation of these many potential variables in a population-based sample.

We therefore assessed the potential predictors of advanced cancer, care at a transplant center, provision of treatment, and mortality among patients from a population-based state registry linked to insurance claims data.

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Materials and Methods

This work was approved by the Biomedical Institutional Review Board at the University of North Carolina (#12-1828).

Patients

The cohort comprised patients diagnosed with HCC in 2003 through 2013, identified from the North Carolina Central Cancer Registry (NCCCR) by ICD-10 code C22.0 and ICD-O-3 histology codes 8170–8175 and 8180. These patients were linked to insurance claims from Medicare, Medicaid, and large private insurance providers in North Carolina by the UNC Lineberger Cancer Information & Population Health Resource.¹⁸ This subset consisted of patients with continuous healthcare enrollment in any health plan for 12 months preceding and 12 months after diagnosis (or death). Patients participating in a Medicare HMO/Advantage plan were excluded because claims are not required to be reported to Medicare.

To evaluate factors associated with treatment and survival, only patients surviving the 90-day exposure window after diagnosis were included in multivariable models, thereby including only patients who may have been eligible for treatment.

Covariates

Patient age, sex, marital status, race, county and zip code of residence, and insurance status at diagnosis were derived from the NCCCR demographics file. We used the NCCCR collaborative staging extension variables of number of tumors and presence/absence of vascular invasion to group cancers into clinically meaningful categories (ie, single or multiple, with or without vascular invasion, and extrahepatic disease). Multifocal cancer was defined as the presence of multiple intrahepatic tumors with or without vascular spread, extrahepatic spread, or unstaged HCC. As has been done in previous studies of HCC outcomes using claims data,⁵ unstaged HCC was considered together with extrahepatic spread given the similar outcomes among these groups. These categories are similar to the tumor extent component of the Barcelona Clinic Liver Cancer staging system and approximate patients who may qualify for liver transplantation, surgical resection, or locoregional therapies.^{19,20}

County-level economic and healthcare covariates were taken from the Area Health Resources File²¹ and the North Carolina Health Professions Data System (<https://nchealthworkforce.unc.edu/>). Measures were selected to cover domains used in other composite measures of census tract–based socioeconomic status.^{22–24} Given the large number of covariates measured across 100

North Carolina counties, we used factor analysis to create representative indices. Factor analysis was conducted separately for health system factors that together had an average variance extracted of 58% across counties and for economic factors (see supplemental eTable 1, available with this article at JNCCN.org). For economic variables, 2 factors combined for an average variance extracted of 83.2% across counties. The first factor was described as an economic disadvantage index because it was dominated by median home value, percentage of White patients, and unemployment rate. The second was described as the rurality index because it was dominated by level of rurality and percentage of agricultural/forestry/hunting/mining industries. For each index, the lowest quartile described the least disadvantaged patients according to these measures.

Additional patient-level covariates were determined from ICD-9 claims in the 12 months prediagnosis, including nonliver comorbidity using the Klabunde modification of the Charlson-Deyo comorbidity index (excluding liver disease),²⁵ psychiatric comorbidity not including substance abuse (eg, depression, anxiety, bipolar disorder, schizophrenia, posttraumatic stress disorder), liver-related complications (eg, encephalopathy, ascites, varices, hepatorenal syndrome),²⁶ and underlying cause of liver disease. Because many patients had low healthcare utilization in the year before diagnosis, codes for the cause of liver disease were evaluated from 12 months before diagnosis to 1 month after diagnosis.

Prediagnosis healthcare utilization was determined by visits with a primary care provider or gastroenterology/hepatology provider in the year before diagnosis (excluding 2 months prediagnosis, when consultations may reflect referrals for cancer), prediagnosis alpha fetoprotein (AFP) screening²⁷ (American Association for the Study of Liver Diseases guidelines recommended every 6 months during this era for patients with cirrhosis and hepatitis virus),²⁸ and number of unique contacts with the healthcare system (inpatient or outpatient visits). Consultation with HCC-specific subspecialty clinicians and at a liver transplant center was measured in the 90 days after diagnosis. Distance from each patient's zip code to the closest liver transplant center was calculated. Treatment was defined as the initial treatment received as described in earlier research,⁵ acknowledging that many patients go on to receive multiple therapies.

Analysis

We extracted patient- and county-level factors for all patients with HCC and linked claims data, and performed univariate analyses on demographic characteristics, insurance status, socioeconomic status, rurality,

medical/psychiatric comorbidities, liver disease etiology and complications, and cancer stage at diagnosis, calculating the median and interquartile range (IQR) for continuous variables and proportions for categorical variables. We calculated annual rates for subspecialty consultation within 90 days of HCC diagnosis and provision of HCC treatments. Multivariable logistic regression analysis was used to assess the variables associated with multifocal cancer at diagnosis, transplant center visits, and provision of HCC treatments. Finally, we developed a Cox proportional hazards model to assess variables associated with overall survival. All statistical analyses were performed with SAS 9.4 (SAS Institute Inc).

Results

Cohort Description

Our cohort included 1,809 patients with HCC (supplemental eFigure 1 and eTable 2). Most patients had single (37%) or multiple (25%) tumors without vascular invasion or extrahepatic spread. A smaller proportion had vascular spread at diagnosis, including 6% and 13% of those with single and multiple lesions, respectively. Median age was 68 years (IQR, 59–76 years) and patients were predominantly male (73%), White (76%), and had Medicare insurance (59%).

Multifocal HCC at Diagnosis

A total of 1,033 patients (57%) had multifocal HCC at presentation. Multifocal cancer at presentation was significantly associated with age, marital status, and sex. Receipt of prediagnosis AFP screening (adjusted odds ratio [aOR], 0.72; 95% CI, 0.58–0.90) and PCP and gastroenterology/hepatology care (aOR, 0.77; 95% CI, 0.61–0.96) was associated with decreased odds of multifocal disease (Table 2).

Visits to a Liver Transplant Center

In the 90 days after diagnosis, 957 (53%) of patients were seen at a liver transplant center for any reason (Figure 1 and eTable 3). A transplant center visit was significantly less likely among patients who were older (age ≥ 75 vs < 50 years: aOR, 0.52; 95% CI, 0.28–0.94), Black (vs White: aOR, 0.54; 95% CI, 0.39–0.74), insured by Medicare (vs private insurance: aOR, 0.35; 95% CI, 0.21–0.59), and insured by Medicaid/dual (vs private insurance: aOR, 0.46; 95% CI, 0.28–0.77).

Patients residing a median of 53 miles (aOR, 0.46; 95% CI, 0.32–0.66) and 106 miles (aOR, 0.27; 95% CI, 0.18–0.41) from the closest transplant center were less likely to have visited a transplant center than those living in the closest tertile (median, 17.4 miles). Transplant center visits were also less likely among those living in the most rural counties (vs least rural: aOR, 0.24; 95% CI,

0.14–0.47). Prediagnosis healthcare was also a major determinant of transplant center visit, with increased odds among patients with more prediagnosis healthcare utilization (highest vs lowest tertile: aOR, 2.14; 95% CI, 1.57–2.93), AFP screening (aOR, 1.74; 95% CI, 1.35–2.23), and gastroenterology/hepatology care (aOR, 1.66; 95% CI, 1.27–2.18).

Provision of HCC Treatment

Of the 1,809 patients with HCC, 30% died within the 90-day treatment exposure window after diagnosis and were excluded from treatment and survival analyses. These patients were older (ie, more likely to be aged ≥ 75 years), had greater comorbidity, had more advanced cancer, were more likely to be divorced, and were less likely to have received prediagnosis care. They were significantly less likely to be seen at a transplant center or to have received treatment for their HCC.

In the 1,250 patients surviving the 90-day treatment exposure window, 857 (69%) were treated (Table 1). The types of treatments used over time can be seen in Figure 2. Of these patients, 478 (56%) had a surgical consultation, 425 (50%) had a gastroenterology/hepatology consultation, and 469 (55%) saw a hematologist/oncologist; these rates slowly increased from 2003 to 2013 (Figure 1).

Factors most strongly associated with receipt of HCC treatment included prediagnosis AFP screening (aOR, 2.61; 95% CI, 1.90–3.60), surgical consultation (aOR, 3.40; 95% CI, 2.48–4.67), and visit to a liver transplant center (aOR, 2.42; 95% CI, 1.74–3.36) (Table 1). In contrast, advanced age (65–74 or ≥ 75 years), unmarried status, psychiatric comorbidity, and liver-related complications all significantly reduced the odds of receiving HCC treatment.

Overall Survival

Across the study period, survival increased from a median of 6 months (IQR, 2–21) in 2004 through 2006 to 8 months (IQR, 2–28) in 2010 through 2012. In adjusted models accounting for disease severity and treatment, patients diagnosed in 2008 and beyond had significantly better survival than those diagnosed in 2004 through 2007 (adjusted hazard ratio [aHR] for death, 0.75; 95% CI, 0.66–0.85).

In addition to year of diagnosis, cancer stage and receipt of cancer treatment were strongly associated with survival. Compared with the 12% of patients who underwent curative surgery, risk of death was higher among those treated with ablation (aHR, 1.60; 95% CI, 1.20–2.13) and locoregional therapy (aHR, 2.47; 95% CI, 1.90–3.19). Patients treated with drug therapy (aHR, 4.57; 95% CI, 3.27–6.40) or radiation (aHR, 3.79; 95% CI, 2.55–5.65) and those who were untreated (aHR, 4.97; 95% CI, 3.79–6.51)

Table 1. Factors Associated With Treatment Among Patients Surviving 90 Days From Diagnosis (N=1,250)

Characteristic	Treated n (%)	Untreated n (%)	Odds of Treatment ^a	
			OR (95% CI)	aOR (95% CI)
Patients, n	857 (69)	393 (31)		
Initial treatment				
Curative surgery	149 (12)	—	—	—
Ablation	186 (15)	—	—	—
LRT (TACE + TARE)	387 (31)	—	—	—
Drug therapy	89 (7)	—	—	—
Radiation	46 (4)	—	—	—
Year of diagnosis				
2004–2005	162 (19)	78 (20)	Ref	Ref
2006–2007	160 (19)	75 (19)	1.03 (0.70–1.51)	0.91 (0.58–1.44)
2008–2009	200 (23)	101 (26)	0.95 (0.66–1.37)	0.86 (0.56–1.33)
2010–2011	208 (24)	77 (20)	1.30 (0.89–1.89)	1.33 (0.85–2.07)
2012–2013	127 (15)	62 (16)	0.99 (0.66–1.48)	1.09 (0.65–1.82)
Median age, y				
<65	382 (45)	134 (34)	Ref	Ref
65–74	306 (36)	112 (28)	0.96 (0.72–1.28)	0.64 (0.41–0.99)
≥75	169 (20)	147 (37)	0.40 (0.30–0.54)	0.30 (0.18–0.49)
Race				
White	661 (77)	289 (74)	Ref	Ref
Black	162 (19)	92 (23)	0.77 (0.58–1.03)	0.84 (0.56–1.24)
Other	34 (4)	12 (3)	1.24 (0.63–2.43)	1.42 (0.64–3.18)
Marital status				
Married	415 (48)	150 (38)	Ref	Ref
Divorced/Separated/Single	239 (28)	173 (44)	0.53 (0.41–0.69)	0.62 (0.44–0.88)
Other/Unknown	203 (24)	70 (18)	0.99 (0.71–1.38)	0.81 (0.53–1.22)
Insurance at diagnosis				
Private	117 (14)	18 (5)	Ref	Ref
Medicare	478 (56)	233 (59)	0.32 (0.19–0.53)	0.78 (0.40–1.50)
Medicaid/Dual	262 (31)	142 (36)	0.28 (0.17–0.49)	0.80 (0.41–1.54)
Psychiatric comorbidity				
No	488 (57)	192 (49)	Ref	Ref
Yes	369 (43)	201 (51)	0.72 (0.57–0.92)	0.64 (0.47–0.89)
CCI score				
0	354 (41)	140 (36)	Ref	Ref
1	266 (31)	108 (27)	0.97 (0.72–1.31)	0.90 (0.63–1.30)
≥2	237 (28)	145 (37)	0.65 (0.49–0.86)	0.78 (0.54–1.12)
Liver-related complications				
0	561 (65)	250 (64)	Ref	Ref
≥1	296 (35)	143 (36)	0.92 (0.72–1.18)	0.51 (0.35–0.74)

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Table 1. Factors Associated With Treatment Among Patients Surviving 90 Days From Diagnosis (cont.)

Characteristic	Treated n (%)	Untreated n (%)	Odds of Treatment ^a	
			OR (95% CI)	aOR (95% CI)
Cancer extension				
Single without vascular invasion	375 (44)	129 (33)	Ref	Ref
Single with vascular invasion	59 (7)	28 (7)	0.72 (0.44–1.19)	0.69 (0.38–1.24)
Multiple without vascular invasion	249 (29)	87 (22)	0.98 (0.72–1.35)	1.07 (0.74–1.54)
Multiple with vascular invasion	88 (10)	52 (13)	0.58 (0.39–0.87)	0.59 (0.37–0.94)
Extrahepatic	20 (2)	15 (4)	0.46 (0.23–0.92)	0.43 (0.19–0.99)
Not staged	66 (8)	82 (21)	0.28 (0.19–0.41)	0.43 (0.28–0.68)
1 y prediagnosis specialty care				
None	86 (10)	65 (17)	Ref	Ref
PCP only	412 (48)	225 (57)	1.38 (0.96–1.99)	1.36 (0.85–2.17)
GE/Hepatology	359 (42)	103 (26)	2.63 (1.78–3.89)	1.68 (0.98–2.86)
1 y prediagnosis AFP screening				
No	354 (41)	267 (68)	Ref	Ref
Yes	503 (59)	126 (32)	3.01 (2.34–3.87)	2.61 (1.90–3.60)
Surgical consult 90 days after diagnosis				
No	379 (44)	295 (75)	Ref	Ref
Yes	478 (56)	98 (25)	3.80 (2.91–4.95)	3.40 (2.48–4.67)
Visit to liver transplant center 90 days from diagnosis				
Yes	659 (77)	183 (47)	3.54 (2.76–4.54)	2.42 (1.74–3.36)
No	198 (23)	210 (53)	Ref	Ref
County economic disadvantage index				
Q1: least disadvantaged	175 (20)	66 (17)	Ref	Ref
Q2	307 (36)	143 (36)	0.81 (0.57–1.14)	0.56 (0.35–0.87)
Q3	277 (32)	135 (34)	0.77 (0.55–1.10)	0.80 (0.50–1.30)
Q4: most disadvantaged	98 (11)	49 (12)	0.75 (0.48–1.18)	0.79 (0.44–1.43)
County rurality index				
Q1: least rural	467 (54)	203 (52)	Ref	Ref
Q2	197 (23)	92 (23)	0.93 (0.69–1.25)	0.90 (0.58–1.39)
Q3	139 (16)	64 (16)	0.94 (0.67–1.32)	0.70 (0.45–1.11)
Q4: most rural	54 (6)	34 (9)	0.69 (0.44–1.09)	0.70 (0.37–1.33)

Abbreviations: AFP, alpha fetoprotein; aOR, adjusted odds ratio; CCI, Charlson-Deyo comorbidity index; GE, gastroenterology; LRT, locoregional therapies; OR, odds ratio; PCP, primary care physician; TACE, transarterial chemoembolization; TARE, transarterial radioembolization; Q, quartile.

^aModel was also adjusted for sex, cause of liver disease, prediagnosis healthcare utilization, postdiagnosis GE/hepatology and hematology/oncology consultation, and county health services index, which were not significantly associated with survival with minimal/no trend suggesting possible effect. These variables were omitted to condense the table size.

had a higher risk of mortality, although these results were not adjusted for factors that may influence treatment selection (eg, bilirubin level) (Table 2).

Survival was better among younger patients (aged <55 years) and those without comorbidities. Receipt of pre-diagnosis gastroenterology/hepatology care was associated with improved survival compared with patients who saw neither a primary care nor a gastroenterology/hepatology physician in the year before diagnosis (aHR, 0.74; 95% CI, 0.58–0.94). Despite adjusting for age and treatment

received, patients with Medicare (aHR, 1.58; 95% CI, 1.20–2.09) and Medicaid/dual (aHR, 1.55; 95% CI, 1.17–2.05) had significantly worse survival than those with private insurance (Table 2).

Discussion

In this population-based retrospective cohort study examining the effects of patient characteristics, county-level resources, and healthcare utilization on HCC outcomes, we found patient-level sociodemographic factors (age

Table 2. Factors Associated With Survival Among Patients Surviving 90 Days From Diagnosis (N=1,250)

Patient-Level Characteristic	Patients Surviving 90 Days n (%)	Hazard for Mortality ^a	
		HR (95% CI)	aHR (95% CI)
Year			
2004–2007	475 (38)	Ref	Ref
2008–2013	775 (62)	0.85 (0.75–0.97)	0.75 (0.66–0.85)
Age, y			
<50	93 (7)	Ref	Ref
50–64	423 (34)	0.97 (0.76–1.26)	1.08 (0.83–1.40)
65–74	418 (33)	1.32 (1.02–1.69)	1.34 (1.00–1.78)
≥75	316 (25)	1.48 (1.15–1.92)	1.39 (1.03–1.87)
Race			
White	950 (76)	Ref	Ref
Black	254 (20)	1.09 (0.94–1.27)	1.09 (0.91–1.30)
Other	46 (4)	0.92 (0.66–1.28)	1.40 (0.98–1.99)
Insurance at diagnosis			
Private	135 (11)	Ref	Ref
Medicare	711 (57)	2.31 (1.82–2.93)	1.58 (1.20–2.09)
Medicaid/Dual	404 (32)	2.50 (1.95–3.20)	1.55 (1.17–2.05)
Psychiatric comorbidity			
No	680 (54)	Ref	Ref
Yes	570 (46)	1.16 (1.03–1.31)	1.15 (1.00–1.32)
CCI score			
0	494 (40)	Ref	Ref
1	374 (30)	1.18 (1.02–1.36)	1.14 (0.97–1.33)
≥2	382 (31)	1.40 (1.21–1.62)	1.18 (1.00–1.38)

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>65 years, Black race, unmarried status, type of insurance) to be key determinants of stage at diagnosis and survival after an HCC diagnosis. These same patient factors were associated with liver transplant center visits and cancer-directed treatment. When further analyzing the root causes, we found that survival was most strongly associated with receipt of cancer-directed treatment. Treatment in turn was more likely in patients with prediagnosis gastroenterology/hepatology specialty care and AFP screening and with post-diagnosis liver transplant center visits, which are likely a surrogate for receipt of multidisciplinary care. The disparities in outcomes were therefore largely accounted for by lower-quality healthcare before and after an HCC diagnosis. In all analyses, Medicaid and Medicare beneficiaries experienced significantly inferior outcomes, including a marked reduction in survival, compared with patients who were privately insured.

Given that HCC incidence is higher among racial and ethnic minorities and in socioeconomically disadvantaged regions,^{29,30} we hypothesized that a lack of access to

local healthcare resources and greater socioeconomic status disadvantage are key contributing factors to the low rates of treatment and the disparities in care that have been previously reported. After investigating a wide array of county-level determinants of economic health and healthcare availability, we found that the only clear associations between county factors and quality of HCC care were that patients residing in the most rural counties and counties farthest from a transplant center were least likely to be seen at a transplant center in the 90 days after diagnosis. No other county-level factors clearly influenced treatment or survival among patients with HCC.

Health insurance was strongly associated with the likelihood of transplant center visits and survival. The association between Medicare insurance and these outcomes could be confounded by age, given that Medicare beneficiaries are usually aged >65 years and some patients may be ineligible for liver transplantation based on advanced age. However, recent data suggest that an increased proportion of patients with HCC

Table 2. Factors Associated With Treatment Among Patients Surviving 90 Days From Diagnosis (cont.)

Patient-Level Characteristic	Patients Surviving 90 Days n (%)	Hazard for Mortality ^a	
		HR (95% CI)	aHR (95% CI)
Liver-related complications			
0	811 (65)	Ref	Ref
≥1	439 (35)	1.00 (0.88–1.14)	1.24 (1.05–1.45)
Cancer extension			
Single lesion	591 (47)	Ref	Ref
Multiple without vascular invasion	336 (27)	1.51 (1.31–1.75)	1.41 (1.21–1.64)
Multiple with vascular invasion	140 (11)	2.18 (1.79–2.66)	1.74 (1.42–2.14)
Extrahepatic/Not staged	183 (15)	2.05 (1.71–2.44)	1.39 (1.15–1.69)
Initial cancer-directed treatment			
Curative surgery	149 (12)	Ref	Ref
Ablation	186 (15)	1.50 (1.14–1.97)	1.60 (1.20–2.13)
LRT (TACE/Y90)	387 (31)	2.68 (2.11–3.41)	2.47 (1.90–3.19)
Drug therapy (including sorafenib)	89 (7)	5.81 (4.28–7.90)	4.57 (3.27–6.40)
Radiation	46 (4)	4.49 (3.10–6.49)	3.79 (2.55–5.65)
Never treated	393 (31)	5.57 (4.38–7.09)	4.97 (3.79–6.51)
1 y prediagnosis specialty care			
None	151 (12)	Ref	Ref
PCP only	637 (51)	0.94 (0.78–1.13)	0.83 (0.67–1.03)
GE/Hepatology	462 (37)	0.68 (0.56–0.83)	0.74 (0.58–0.94)
Hematology/Oncology consult			
No	562 (45)	Ref	Ref
Yes	688 (55)	1.53 (1.36–1.73)	1.39 (1.21–1.59)

Abbreviations: aHR, adjusted hazard ratio; CCI, Charlson-Deyo comorbidity index; GE, gastroenterology; HR, hazard ratio; LRT, locoregional therapies; PCP, primary care physician; TACE, transarterial chemoembolization; Y90, yttrium-90.

^aModel was also adjusted for sex, marital status, cause of liver disease, prediagnosis healthcare utilization, prediagnosis alpha fetoprotein screening, surgical or GE/hepatology consult in 90 days of diagnosis, NCI center or liver transplant center visit in 90 days after diagnosis, and county-level economic, rurality, and health services disadvantage indices, which were not significantly associated with survival with minimal/no trend suggesting possible effect. These variables were omitted to condense the table size.

aged >65 years are being listed for transplantation,³¹ and the negative associations between Medicare insurance and transplant center visits and survival persisted in multivariable models adjusting for age. Patients with Medicare and Medicaid had a 24% and 57% increased risk of death, respectively, compared with those with private insurance; this risk was 67% higher for those who were uninsured. The effect of insurance status on survival did not diminish after adjusting for patient age, comorbidity, and treatment, with a 58% and 55% increase in risk of death for patients with Medicare and Medicaid, respectively. The influence of public insurance on outcomes could reflect limitations imposed by Medicare and Medicaid on access to care; however, public insurance in this analysis is also likely a proxy for individual socioeconomic resources, given that income limits for North Carolina Medicaid are strict.³² Regardless of county resources, individuals with Medicare or Medicaid likely face additional financial challenges

that could compromise access compared with their privately insured counterparts. The marked and persistently inferior outcomes among patients who were single, divorced/separated, or widowed (ie, advanced stage at presentation, less consultative care and treatment) and those with psychiatric comorbidity (ie, lower rates of treatment and inferior survival) also speak to the importance of individual resources (eg, social support) on the ability of patients with HCC to receive the care they need.

This study is strengthened by its large population-based sample and the availability of linked insurance claims, allowing for the simultaneous exploration of patient, treatment, and facility factors on outcomes. However, this study must be interpreted in the context of potential limitations. First, the survival analysis was limited to patients who survived the 90-day treatment exposure window after diagnosis. Although this restriction was necessary to evaluate the effect of treatment on

Figure 1. Time trends of subspecialty consultation within 90 days of diagnosis among incident patients with HCC diagnosed between 2004 and 2012.

Abbreviations: GE, gastroenterology; HCC, hepatocellular carcinoma; Hem/Onc, hematology/oncology.

survival, omitting these sickest patients may have obscured the effect of county economic and healthcare factors on HCC outcomes. Although we generally found that the same factors that were associated with treatment were associated with early mortality (ie, age >65 years and cancer stage, greater comorbidity, single/divorced/separated status, Medicare/Medicaid insurance, less prediagnostic care), a potentially meaningful difference was that patients with early mortality were more likely to live in a county with fewer healthcare services and lower density of gastroenterology/hepatology physicians. Second, the data source did not allow for adjustment for liver disease severity via the Model for End-Stage Liver Disease or Child-Pugh score, although we did account for prediagnosis liver-related complications. Finally, our data source did not allow us to assess for factors that could have contributed to improved survival over time, including improved treatments for underlying liver disease (eg, direct-acting antiviral therapy for hepatitis C virus), expanded access to HCC therapies and clinical trials, and broader adoption of multidisciplinary tumor boards and clinics.

Conclusions

Our findings that an individual's use of the healthcare system before diagnosis and visits to an expert center early during the cancer course are major driving forces behind treatment and survival for HCC are critical when considering how to improve outcomes of patients with HCC—both in North Carolina and across the nation. To reduce the rates of very early mortality from HCC, public health efforts must focus on detection of cirrhosis

Figure 2. Time trends of type of initial treatment received by year of diagnosis among incident patients with HCC diagnosed between 2004 and 2012. Most patients diagnosed with HCC received no treatment every year during the study period.

Abbreviations: HCC, hepatocellular carcinoma; TACE, transarterial chemo-embolization; Y90, yttrium-90.

and gastroenterology/hepatology referrals for affected individuals. To improve survival among patients who present earlier in their disease course, efforts must focus on increasing access to subspecialty care and treatment. Our ongoing work will examine patient-reported barriers to accessing care after an HCC diagnosis, with a focus on high-risk Black and rural residents and Medicare and Medicaid beneficiaries.

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References

- White DL, Thrift AP, Kanwal F, et al. Incidence of hepatocellular carcinoma in all 50 United States, from 2000 through 2012. *Gastroenterology* 2017; 152:812–820.e5.
- Petrick JL, Kelly SP, Altekruse SF, et al. Future of hepatocellular carcinoma incidence in the United States forecast through 2030. *J Clin Oncol* 2016; 34:1787–1794.
- Kohler BA, Sherman RL, Howlander N, et al. Annual report to the nation on the status of cancer, 1975–2011, featuring incidence of breast cancer subtypes by race/ethnicity, poverty, and state. *J Natl Cancer Inst* 2015; 107:djv048.
- El-Serag HB, Siegel AB, Davila JA, et al. Treatment and outcomes of treating of hepatocellular carcinoma among Medicare recipients in the United States: a population-based study. *J Hepatol* 2006;44: 158–166.
- Sanoff HK, Chang Y, Stavas JM, et al. Effectiveness of initial transarterial chemoembolization for hepatocellular carcinoma among Medicare beneficiaries. *J Natl Compr Canc Netw* 2015;13:1102–1110.
- Davila JA, Kramer JR, Duan Z, et al. Referral and receipt of treatment for hepatocellular carcinoma in United States veterans: effect of patient and nonpatient factors. *Hepatology* 2013;57:1858–1868.
- Shah SA, Smith JK, Li Y, et al. Underutilization of therapy for hepatocellular carcinoma in the Medicare population. *Cancer* 2011;117:1019–1026.
- Lopez PM, Villanueva A, Llovet JM. Systematic review: evidence-based management of hepatocellular carcinoma—an updated analysis of randomized controlled trials. *Aliment Pharmacol Ther* 2006;23:1535–1547.
- Wang J, Ha J, Lopez A, et al. Medicaid and uninsured hepatocellular carcinoma patients have more advanced tumor stage and are less likely to receive treatment. *J Clin Gastroenterol* 2018;52:437–443.
- Mokdad AA, Zhu H, Marrero JA, et al. Hospital volume and survival after hepatocellular carcinoma diagnosis. *Am J Gastroenterol* 2016; 111:967–975.
- Tan D, Yopp A, Beg MS, et al. Meta-analysis: underutilization and disparities of treatment among patients with hepatocellular carcinoma in the United States. *Aliment Pharmacol Ther* 2013;38:703–712.
- Artinyan A, Mailey B, Sanchez-Luege N, et al. Race, ethnicity, and socioeconomic status influence the survival of patients with hepatocellular carcinoma in the United States. *Cancer* 2010;116:1367–1377.
- Davila JA, El-Serag HB. Racial differences in survival of hepatocellular carcinoma in the United States: a population-based study. *Clin Gastroenterol Hepatol* 2006;4:104–110.
- Siegel AB, McBride RB, El-Serag HB, et al. Racial disparities in utilization of liver transplantation for hepatocellular carcinoma in the United States, 1998–2002. *Am J Gastroenterol* 2008;103:120–127.
- Davila JA, Duan Z, McGlynn KA, et al. Utilization and outcomes of palliative therapy for hepatocellular carcinoma: a population-based study in the United States. *J Clin Gastroenterol* 2012;46:71–77.
- Rich NE, Hester C, Odewole M, et al. Racial and ethnic differences in presentation and outcomes of hepatocellular carcinoma. *Clin Gastroenterol Hepatol* 2019;17:551–559.e1.
- Serper M, Taddei TH, Mehta R, et al. Association of provider specialty and multidisciplinary care with hepatocellular carcinoma treatment and mortality. *Gastroenterology* 2017;152:1954–1964.
- Meyer AM, Olshan AF, Green L, et al. Big data for population-based cancer research: the integrated cancer information and surveillance system. *N C Med J* 2014;75:265–269.
- Forner A, Reig ME, de Lope CR, et al. Current strategy for staging and treatment: the BCLC update and future prospects. *Semin Liver Dis* 2010;30:61–74.
- Llovet JM, Brú C, Bruix J. Prognosis of hepatocellular carcinoma: the BCLC staging classification. *Semin Liver Dis* 1999;19:329–338.
- Health Resources & Services Administration. Area Health Resources Files. Accessed July 28, 2020. Available at: <http://data.hrsa.gov/topics/health-workforce/ahrf>
- Yu M, Tatalovich Z, Gibson JT, et al. Using a composite index of socioeconomic status to investigate health disparities while protecting the confidentiality of cancer registry data. *Cancer Causes Control* 2014;25:81–92.
- Yost K, Perkins C, Cohen R, et al. Socioeconomic status and breast cancer incidence in California for different race/ethnic groups. *Cancer Causes Control* 2001;12:703–711.
- Krieger N, Chen JT, Waterman PD, et al. Geocoding and monitoring of US socioeconomic inequalities in mortality and cancer incidence: does the choice of area-based measure and geographic level matter? The Public Health Disparities Geocoding Project. *Am J Epidemiol* 2002;156: 471–482.
- Klabunde CN, Potosky AL, Legler JM, et al. Development of a comorbidity index using physician claims data. *J Clin Epidemiol* 2000; 53:1258–1267.
- Ulahannan SV, Duffy AG, McNeel TS, et al. Earlier presentation and application of curative treatments in hepatocellular carcinoma. *Hepatology* 2014;60:1637–1644.
- Davila JA, Morgan RO, Richardson PA, et al. Use of surveillance for hepatocellular carcinoma among patients with cirrhosis in the United States. *Hepatology* 2010;52:132–141.
- Bruix J, Sherman M. Management of hepatocellular carcinoma: an update. *Hepatology* 2010;53:1020–1022.
- Shebl FM, Capo-Ramos DE, Graubard BI, et al. Socioeconomic status and hepatocellular carcinoma in the United States. *Cancer Epidemiol Biomarkers Prev* 2012;21:1330–1335.
- Chang ET, Yang J, Alfaro-Velcamp T, et al. Disparities in liver cancer incidence by nativity, acculturation, and socioeconomic status in California Hispanics and Asians. *Cancer Epidemiol Biomarkers Prev* 2010;19:3106–3118.
- Cullaro G, Rubin JB, Mehta N, et al. Differential impact of age among liver transplant candidates with and without hepatocellular carcinoma. *Liver Transpl* 2020;26:349–358.
- NC Medicaid Division of Health Benefits. Eligibility for Medicaid or Health Choice. Accessed July 28, 2020. Available at: <http://medicaid.ncdhhs.gov/beneficiaries/get-started/eligibility-medicaid-or-health-choice>

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Supplemental online content for:

Medicare/Medicaid Insurance, Rurality, and Black Race Associated With Provision of Hepatocellular Carcinoma Treatment and Survival

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eFigure 1: CONSORT Diagram of Cohort Assembly

eTable 1: Factor Analysis for Area-Level Indices

eTable 2: Patient Characteristics

eTable 3: Association of Stage at Presentation and Transplant Center Visit With Patient- and Area-Level Factors

eFigure 1. CONSORT diagram of cohort assembly.
Abbreviation: HCC, hepatocellular carcinoma.

eTable 1. Factor Analysis for Area-Level Indices

Variable	Economic Index	Rurality Index	Healthcare Index
Median home value	0.78567	−0.16994	NA
Percentage of White patients	0.74240	0.00694	NA
Median household income	0.56927	−0.52099	NA
Percentage of uninsured patients aged <65 years	0.53235	0.51554	NA
Persistent poverty	−0.49136	0.17469	NA
Lower education level (>25% without high school)	−0.60946	0.24739	NA
High poverty	−0.69429	0.44694	NA
Unemployment rate, age ≥16 years	−0.73858	0.10738	NA
Rural–Urban Continuum Codes	−0.16917	0.77060	NA
Percentage agriculture/forestry/fishing/hunting/mining industries	−0.28463	0.59780	NA
Percentage of Hispanic patients	−0.01373	−0.02848	NA
Percentage of variance explained	54.9	28.3	NA
Internal medicine subspecialties, total patient care per 100,000 population	NA	NA	0.83506
Psychiatric care per 100,000 population	NA	NA	0.80305
Primary care physicians per 100,000 population	NA	NA	0.73967
Short-term hospital beds per 100,000 population	NA	NA	0.65049
Percentage of variance explained	NA	NA	57.8

Abbreviation: NA, not applicable.

eTable 2. Patient Characteristics (N=1,809)

Characteristic	n (%)
Cancer extent	
Single without vascular invasion	671 (37)
Single with vascular invasion	105 (6)
Multiple without vascular invasion	458 (25)
Multiple with vascular invasion	230 (13)
Extrahepatic	66 (4)
Not staged	279 (15)
Median age (IQR), y	68 (59–76)
<50 y	110 (6)
50–64 y	574 (32)
65–74 y	611 (34)
≥75 y	514 (28)
Sex	
Male	1,326 (73)
Female	483 (27)
Race	
White	1,375 (76)
Black	368 (20)
Asian	^a
Native American	^a
Other	66 (4)
Marital status	
Married	803 (44)
Widowed	33 (2)
Divorced/Separated/Single	640 (35)
Other/Unknown	333 (18)
Insurance at diagnosis	
Private	165 (9)
Medicare	1,069 (59)
Medicaid/Dual	575 (32)
Tricare/VA	NA ^b
Other	NA ^b
Uninsured	NA ^b

(continued)

eTable 2. Patient Characteristics (N=1,809) (cont.)

Characteristic	n (%)
Psychiatric comorbidity	
Yes	820 (45)
No	989 (55)
CCI score	
0	657 (36)
1	526 (29)
≥2	626 (35)
Liver-related complications	
0	1,107 (61)
≥1	702 (39)
Cause of liver disease ^c	
Hepatitis B virus	96 (5)
Hepatitis C virus	538 (30)
Alcohol	306 (17)
Other cause of cirrhosis	371 (21)
County economic disadvantage index	
Q1: least disadvantaged	352 (19)
Q2	645 (36)
Q3	595 (33)
Q4: most disadvantaged	216 (12)
County rurality index	
Q1: least rural	953 (53)
Q2	433 (24)
Q3	290 (16)
Q4: most rural	132 (7)
County healthcare disadvantage index	
Q1: least disadvantaged	897 (50)
Q2	389 (22)
Q3	308 (17)
Q4: most disadvantaged	214 (12)

Abbreviations: CCI, Charlson-Deyo Comorbidity Index; IQR, interquartile range; NA, not available; Q, quartile; VA, U.S. Department of Veterans Affairs. ^aTo preserve confidentiality, table cells representing <11 individuals were not included.

^bClaims not available for these insurers.

^cCauses of liver disease are not mutually exclusive and will not sum to 100%.

eTable 3. Association of Stage at Presentation and Transplant Center Visit With Patient- and Area-Level Factors

Characteristic	All Patients With HCC n (%)	Multifocal Cancer n (%)	Odds of Multifocal Cancer aOR (95% CI) ^a	Transplant Center Visit n (%)	Odds of Transplant Center Visit aOR (95% CI) ^a
Patients, N	1,809	1,033		957	
Cancer extension					
Single without vascular invasion	671 (37)	NA	NA	388 (41)	Ref
Multiple without vascular invasion	458 (25)	NA	NA	263 (27)	0.98 (0.74–1.31)
Single with vascular invasion	105 (6)	NA	NA	71 (7)	1.92 (1.16–3.18)
Multiple with vascular invasion	230 (13)	NA	NA	116 (12)	0.83 (0.58–1.19)
Extrahepatic	66 (4)	NA	NA	28 (3)	0.70 (0.39–1.26)
Not staged	279 (15)	NA	NA	91 (10)	0.34 (0.24–0.49)
Age, median (IQR), y	68 (59–76)			66 (57–73)	
<50 y	110 (6)	55 (5)	Ref	75 (8)	Ref
50–64 y	574 (32)	324 (31)	1.31 (0.85–2.00)	354 (37)	0.81 (0.48–1.37)
65–74 y	611 (34)	365 (35)	1.91 (1.19–3.06)	333 (35)	0.95 (0.54–1.69)
≥75 y	514 (28)	289 (28)	1.64 (1.01–2.68)	195 (20)	0.52 (0.28–0.94)
Sex					
Male	1,326 (73)	779 (75)	Ref	715 (75)	Ref
Female	483 (27)	254 (25)	0.74 (0.59–0.93)	242 (25)	0.95 (0.73–1.23)
Race					
White	1,375 (76)	763 (74)	Ref	744 (78)	Ref
Black	368 (20)	232 (22)	1.22 (0.93–1.61)	174 (18)	0.54 (0.39–0.74)
Other	66 (4)	38 (4)	1.05 (0.62–1.80)	39 (4)	0.62 (0.32–1.20)
Marital status					
Married	803 (44)	429 (42)	Ref	427 (45)	Ref
Widowed	33 (2)	21 (2)	1.54 (0.73–3.25)	18 (2)	0.68 (0.29–1.58)
Divorced/Separated/Single	640 (35)	388 (38)	1.37 (1.08–1.72)	280 (29)	0.71 (0.54–0.92)
Other/Unknown	333 (18)	195 (19)	1.26 (0.96–1.65)	232 (24)	2.12 (1.52–2.98)
Insurance at diagnosis					
Private	165 (9)	87 (8)	Ref	129 (13)	Ref
Medicare	1,069 (59)	604 (58)	0.89 (0.60–1.33)	519 (54)	0.35 (0.21–0.59)
Medicaid/Dual	575 (32)	342 (33)	1.00 (0.68–1.48)	309 (32)	0.46 (0.28–0.77)
CCI score					
0	657 (36)	389 (38)	Ref	377 (39)	Ref
1	526 (29)	299 (29)	0.95 (0.75–1.22)	283 (30)	0.80 (0.60–1.07)
≥2	626 (35)	345 (33)	0.85 (0.67–1.09)	297 (31)	0.63 (0.48–0.85)
Cause of liver disease ^b					
Hepatitis B virus	96 (5)	54 (5)	1.05 (0.67–1.64)	62 (6)	1.36 (0.80–2.33)
Hepatitis C virus	538 (30)	304 (29)	1.16 (0.89–1.52)	360 (38)	1.72 (1.25–2.36)
Alcohol	306 (17)	174 (17)	1.09 (0.81–1.48)	187 (20)	1.09 (0.76–1.56)
Other cause of cirrhosis	371 (21)	203 (20)	1.03 (0.78–1.36)	208 (22)	1.35 (0.98–1.87)
Prediagnosis healthcare utilization, median encounters (Q1, Q3)					
T1: 1 (0, 2)	526 (29)	326 (32)	Ref	216 (23)	Ref
T2: 5 (3, 6)	657 (36)	377 (36)	0.95 (0.74–1.21)	352 (37)	1.45 (1.09–1.94)
T3: 12 (9, 16)	626 (35)	330 (32)	0.86 (0.66–1.12)	389 (41)	2.14 (1.57–2.93)

(continued on next page)

Table 3. Association of Stage at Presentation and Transplant Center Visit With Patient- and Area-Level Factors (cont.)

Characteristic	All Patients With HCC n (%)	Multifocal Cancer n (%)	Odds of Multifocal Cancer aOR (95% CI) ^a	Transplant Center Visit n (%)	Odds of Transplant Center Visit aOR (95% CI) ^a
1 y prediagnosis specialty care					
None	245 (14)	725 (70)	Ref	419 (44)	Ref
PCP only	951 (53)	c	c	c	c
PCP + GE/hepatology	567 (31)	308 (30)	0.77 (0.61–0.96)	538 (56)	1.66 (1.27–2.18)
GE/Hepatology only	46 (3)	c	c	c	c
1 y prediagnosis AFP screening					
Yes	779 (43)	398 (39)	0.72 (0.58–0.90)	521 (54)	1.74 (1.35–2.23)
No	1,030 (57)	635 (61)	Ref	436 (46)	Ref
Miles to closest transplant center, median (Q1, Q3)					
T1: 17.4 (7.3, 25.3)	605 (33)	346 (34)	NA	442 (46)	Ref
T2: 53 (44.2, 60.8)	602 (33)	354 (34)	NA	268 (28)	0.46 (0.32–0.66)
T3: 106 (90, 133)	600 (33)	331 (32)	NA	247 (26)	0.27 (0.18–0.41)
County economic disadvantage index					
Q1: least disadvantaged	352 (19)	185 (18)	Ref	164 (17)	Ref
Q2	645 (36)	369 (36)	1.13 (0.85–1.51)	427 (45)	0.96 (0.65–1.41)
Q3	595 (33)	337 (33)	1.06 (0.77–1.45)	248 (26)	0.36 (0.24–0.56)
Q4: most disadvantaged	216 (12)	141 (14)	1.50 (1.01–2.23)	118 (12)	1.76 (1.10–2.83)
County rurality index					
Q1: least rural	953 (53)	550 (53)	Ref	553 (58)	Ref
Q2	433 (24)	240 (23)	0.87 (0.65–1.77)	214 (22)	0.56 (0.39–0.81)
Q3	290 (16)	165 (16)	0.89 (0.65–1.20)	158 (17)	1.28 (0.84–1.96)
Q4: most rural	132 (7)	77 (7)	0.90 (0.58–1.39)	32 (3)	0.24 (0.14–0.47)
County healthcare disadvantage index					
Q1: least disadvantaged	853 (47)	478 (46)	Ref	469 (49)	Ref
Q2	441 (24)	258 (25)	1.06 (0.81–1.39)	241 (25)	0.98 (0.70–1.37)
Q3	296 (16)	164 (16)	1.04 (0.78–1.38)	151 (16)	1.01 (0.70–1.45)
Q4: most disadvantaged	218 (12)	132 (13)	1.21 (0.86–1.71)	96 (10)	0.73 (0.48–1.10)

Abbreviations: AFP, alpha fetoprotein; aOR, adjusted odds ratio; CCI, Charlson-Deyo comorbidity index; GE, gastroenterology; HCC, hepatocellular carcinoma; IQR, interquartile ratio; NA, not available; PCP, primary care physician; T, tertile; Q, quartile.

^aModel was also adjusted for psychiatric comorbidity, liver comorbidity (complications of cirrhosis), and number of hepatologists per 100,000 population, which was not significantly associated with survival with minimal/no trend suggesting possible effect. These variables were omitted to condense the table size.

^bCauses of liver disease are not mutually exclusive and will not sum to 100%.

^cCells combined with cell above for multivariable model, comparing “any GI/hepatology” to referent of “none” or “PCP only.”