Effect of Hospital Safety Net Designation on Treatment Use and Survival in Hepatocellular Carcinoma

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BACKGROUND: Racial/ethnic minorities with hepatocellular carcinoma (HCC) have worse survival than non-Hispanic whites. Comparing patient outcomes across health care delivery systems can identify biological and care delivery mechanisms contributing to this disparity. We compared presentation, treatment, and survival of HCC patients treated at safety net hospitals (SNHs) and non-SNHs.

METHODS: Patients diagnosed with HCC from 2001 to 2012 were identified in the Texas Cancer Registry. We compared hospital and patient characteristics across three hospital categories: non-SNHs, low-proportion SNHs (l-SNHs), and high-proportion SNHs (h-SNHs). Covariate-adjusted treatment use and overall survival were compared among the 3 hospital categories.

RESULTS: Despite comprising only 23% of hospitals, h-SNHs cared for 42% of 17,489 HCC patients and disproportionately delivered care to racial/ethnic minorities and patients of low socioeconomic status compared with non-SNHs. Compared with non-SNHs, treatment use was similar at l-SNHs (45% vs 45%; adjusted odds ratio [OR], 0.97; 95% confidence interval [CI], 0.89-1.06) but significantly lower at h-SNHs (32% vs 45%; OR, 0.64; 95% CI, 0.57-0.73). Similarly, patients with localized HCC were less likely to undergo curative treatment at h-SNHs than non-SNHs (OR, 0.51; 95% CI, 0.40-0.66). Compared with non-SNHs, overall survival was similar at l-SNHs (hazard ratio [HR], 0.93; 95% CI, 0.89-0.98) but significantly worse at h-SNHs (HR, 1.30; 95% CI, 1.22-1.39).

CONCLUSION: Patients at SNHs are less likely to undergo HCC treatment, even when diagnosed at an early stage, which likely contributes to worse survival. System-level differences in care delivery may partly explain racial/ethnic and socioeconomic disparities in HCC prognosis.

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KEYWORDS: liver neoplasms, survival, race/ethnicity, disparity.

INTRODUCTION

Hepatocellular carcinoma (HCC) is the third most common cause of cancer death worldwide and the fastest growing cause of cancer death in the United States.1 The incidence of HCC in the United States nearly doubled over the past 2 decades and is anticipated to continue to increase over the next 20 years.2 Within the mainland United States, the incidence of HCC is highest in the state of Texas.3

HCC disproportionately impacts racial/ethnic minorities, who consistently experience higher incidence and worse survival than non-Hispanic whites. Incidence is highest among Hispanics and Asians, and blacks have the worst survival compared with all other racial/ethnic groups.2-4 Racial/ethnic disparities are partly attributable to differences in HCC risk factors and tumor biology; however, variations in delivery of cancer care may also contribute to survival differences.5-7

Safety net hospitals (SNHs) play an integral role caring for cancer patients in the United States, delivering a disproportionate amount of care to the under- and uninsured, Medicaid recipients, and other vulnerable patient populations.8 Understanding how SNHs deliver cancer care for patients with HCC is particularly important because low socioeconomic status and racial/ethnic minority patients receive most of their hospital-based care at SNHs.9,10

Under the Patient Protection and Affordable Care Act, SNHs are expected to provide services to a growing population of newly insured patients, taxing an already overwhelmed system with limited resources.11 Given the rapidly growing HCC incidence and the future uncertainty of SNHs in an evolving healthcare climate, it is important to characterize HCC presentation, treatment, and survival of this population. In this study, we compared differences in the treatment and survival of HCC patients treated at SNHs and non-SNHs.
MATERIALS AND METHODS

Data Sources
Data were obtained from 3 sources: the American Hospital Association (AHA) survey, the Centers for Medicare and Medicaid Services (CMS) impact files, and the Texas Cancer Registry (TCR). The AHA survey collects annual information on US hospitals, including hospital organizational structure, accreditation, services and resources, utilization and expenses, staffing, and geographic indicators. The CMS impact files contain indices for payment adjustments to eligible hospitals and were used to identify SNHs. TCR is a statewide database of demographic, clinical, and hospital data on all incident cancer cases diagnosed in the state of Texas. By legislative mandate, all providers treating patients with a primary diagnosis of cancer are required to report patients to TCR, resulting in nearly 98% case ascertainment. The TCR data currently meet Centers for Disease Control and Prevention quality standards and has gold certification from the North American Association of Central Cancer Registries. We requested and received data that identified the facility at which each patient was seen and a report was made. The resulting dataset—having detailed patient and hospital data including comprehensive hospital reimbursement information—helped generate a comprehensive representation of the complex health care delivery system in Texas.

Hospital Characteristics
Hospital characteristics were derived from the AHA survey. We included all acute short-term hospitals and excluded long-term care facilities, designated children’s hospitals, outpatient centers, and federally owned institutions. Information about hospital location, teaching status, cancer program accreditation, oncology resources, radiology resources, liver transplant capability, total bed number, total annual admissions and Medicare and Medicaid discharges is available from the AHA data. Geographic location was divided into metropolitan, micropolitan, and rural. Members of the Council of Teaching Hospitals of the Association of the American Medical Colleges were designated as major teaching hospitals. Nonmember hospitals that supported an approved residency training program or were affiliated with a medical school were designated as minor teaching hospitals. Oncology resources included an oncology service, palliative care services, and the capability to administer chemotherapeutic drugs. Information on radiology resources including computed tomography scanners, magnetic resonance imaging devices, ultrasound machines, and image-guided radiotherapy was recorded. Hospitals with an approved liver transplantation program were identified from the Organ Procurement and Transplantation Network.

Safety net designation was assigned according to each hospital’s disproportionate share hospital (DSH) index value, extracted from CMS impact files. The DSH index is calculated annually by CMS and reflects the percentage of Medicaid and low-income Medicare patients of the total number of patients treated at a hospital. Hospitals with DSH index values in the upper 25th percentile in a fiscal year were designated as SNHs. According to this definition, approximately 15% of hospitals shifted between SNH and non-SNH designations, because the DSH index values for each hospital change over time. For those hospitals, safety net designation was determined by the number of years a hospital was classified as an SNH; hospitals that met the criteria for SNH for more years than not during the study period were designated as SNHs.

Given the variability in DSH index values among SNHs, we further subcategorized SNHs into low-proportion and high-proportion safety net groups using Contal and O’Quigley’s outcome-based method. According to this method, we identified the upper 10th percentile of the DSH index as a cutpoint that maximizes the difference in overall survival among SNHs (see Supporting Information for details). Therefore, SNHs with DSH index values between the upper 25th and 10th percentiles were designated as low-proportion SNHs (l-SNHs), and SNHs in the upper 10th percentile of DSH index values were designated high-proportion SNHs (h-SNHs). For hospitals that shifted between l-SNH and h-SNH status during the study period, high and low-proportion SNH designation was adjudicated in a similar manner to that used above for determining SNH and non-SNH.

Patient Characteristics
Patients > 18 years of age diagnosed with HCC (International Classification of Diseases for Oncology, 3rd edition, topography code C22.0) between 2001 and 2012 were identified in the TCR. Patients who were diagnosed at autopsy or for whom only a death certificate was available were excluded. Patient demographic data included patients’ age, sex, race and ethnicity, poverty index, and insurance type. Poverty index is a census tract-level measure of the proportion of persons living at or below the federal poverty line. Insurance type was categorized as private insurance, Medicaid, Medicare, military-affiliated, and no insurance. Tumor characteristics included tumor
stage, tumor size, and lymph node involvement. Stage was recorded based on the Surveillance, Epidemiology, and End Results Program (SEER) classification: 1) localized disease is limited to one liver lobe regardless of vascular invasion, 2) regional disease involves more than 1 lobe or invasion of local organs, and 3) distant (ie, metastatic) disease involving lymph nodes or distant organs. Treatment data in the TCR comprised a first course of HCC-directed treatment and included surgical resection, liver transplantation, local ablative therapies, and chemotherapy. We denoted curative HCC treatment as resection, transplantation, or ablation. Chemotherapy included chemoembolization and systemic therapies administered intravenously or orally. Details regarding mode of chemotherapy delivery were not provided. Vital status and date of death were also collected from the TCR.

Patients were categorized according to the safety net designation of the hospital (or hospitals) where they received care. Because the TCR includes up to 9 different hospitals involved in a patient’s care, we created 4 mutually exclusive patient groups: 1) patients treated at non-SNHs exclusively, 2) patients treated at l-SNHs exclusively, 3) patients treated at h-SNHs exclusively, and 4) patients treated at hospitals with more than 1 safety net designation. For example, a patient who was diagnosed at an l-SNH hospital but received treatment at a different and h-SNH hospital was assigned to patient group 4. Similarly, a patient receiving care at 2 different non-SNH hospitals was assigned to patient group 1.

### Statistical Analysis

We first compared hospital characteristics by safety-net designation. We then compared patient demographics and clinical and tumor characteristics among patients who exclusively sought care at hospitals with the same safety-net designation (ie, patient groups 1, 2, and 3 only). We purposefully excluded patients receiving care at more than 1 hospital type (patient group 4, n = 1557) to avoid overlap among the hospital categories. The characteristics of patient group 4 are shown in Supporting Table 1.

Analysis of variance and Pearson’s chi-square test were used to compare continuous and categorical data, respectively. We examined the proportion of patients receiving treatment overall by hospital safety net designation and by tumor stage. A multivariable logistic regression model was used to evaluate factors associated with treatment use among patients treated at non-SNHs, l-SNHs, and h-SNHs. Overall survival was estimated using Kaplan-Meier methods, and a log-rank test was used to compare survival. Adjusted overall survival among patient

### TABLE 1. Characteristics of 328 Acute Short-Term Care Hospitals Caring for HCC Patients in Texas by Safety Net Designation, 2001-2012

| Characteristics                              | Non-SNH (n = 254) | l-SNH (n = 49) | h-SNH (n = 25) | P     |
|----------------------------------------------|-------------------|----------------|----------------|-------|
| Location, n (%)                              |                   |                |                | .17   |
| Rural                                        | 73 (29)           | 8 (16)         | 4 (16)         |       |
| Micropolitan                                 | 32 (13)           | 9 (18)         | 2 (8)          |       |
| Metropolitan                                 | 149 (59)          | 32 (65)        | 19 (76)        |       |
| Teaching, n (%)                              |                   |                |                | <.01  |
| None                                         | 210 (83)          | 30 (61)        | 15 (60)        |       |
| Minor                                        | 38 (15)           | 13 (27)        | 7 (28)         |       |
| Major                                        | 6 (2)             | 6 (12)         | 3 (12)         |       |
| ACS accredited cancer program, n (%)         | 55 (22)           | 14 (29)        | 3 (12)         | .25   |
| Median total bed number (IQR)                | 70 (28-191)       | 86 (32-360)    | 200 (85-318)   | .03   |
| Median annual HCC volume (IQR)               | 2 (1-4)           | 3 (1-9)        | 6 (2-11)       | .04   |
| Oncology resources, n (%)                   |                   |                |                | <.01  |
| Oncology service                             | 123 (48)          | 20 (41)        | 13 (52)        | .56   |
| Administration of chemotherapy               | 105 (41)          | 22 (45)        | 14 (56)        | .35   |
| Palliative care service                      | 64 (25)           | 19 (39)        | 5 (20)         | .11   |
| Hospice                                      | 45 (18)           | 9 (18)         | 5 (20)         | .96   |
| Liver transplantation program, n (%)         | 16 (6)            | 6 (12)         | 3 (12)         | .25   |
| Radiology resources, n (%)                  |                   |                |                | <.01  |
| Computed tomography                          | 242 (95)          | 48 (98)        | 23 (92)        | .50   |
| Magnetic resonance imaging                   | 188 (74)          | 38 (78)        | 20 (80)        | .73   |
| Ultrasound                                   | 231 (91)          | 49 (100)       | 22 (88)        | .07   |
| Image-guided radiation therapy               | 35 (14)           | 6 (12)         | 2 (8)          | .70   |
| Median Medicare discharges, % (IQR)          | 49 (40-59)        | 41% (33-45)    | 32% (28-42)    | <.01  |
| Median Medicaid discharges, % (IQR)          | 13 (7-19)         | 28% (22-35)    | 38% (34-43)    | <.01  |

Abbreviations: ACS, American College of Surgeons; HCC, hepatocellular carcinoma; h-SNH, high-proportion safety net hospital; IQR, interquartile range; l-SNH, low-proportion safety net hospital; non-SNH, non–safety net hospital.
groups was examined using a multivariable Cox proportional hazards model. We adjusted for year of diagnosis, patient demographics (including age, sex, and race), poverty category, tumor characteristics, and treatment receipt. Interaction effects among predictor variables were tested. We evaluated for multicollinearity using the variance inflation factor as well as qualitative assessments. The proportional hazards assumption of the Cox model was evaluated using plots of scaled Schoenfeld residuals. The proportional hazards assumption was reasonable for all predictor variables.

Patients with poor liver function and/or multiple comorbidities are less likely to receive HCC-directed therapy and have worse survival. To account for limited data on liver function and comorbidity, we used conditional landmark analysis to examine differences in treatment receipt and overall survival among patients surviving at least 2 months after diagnosis (n = 10,703), which likely excluded most patients with significant liver dysfunction or comorbidity.21 By excluding those patients, we effectively mitigated (at least partially) the impact of extremely poor liver function on differences in treatment receipt and overall survival among SNH categories. More broadly, this method also helps mitigate concerns about differential risk due to underlying health status between SNHs and non-SNHs.

We conducted a sensitivity analysis using propensity score weighting to evaluate association of SNH designation and survival among patients balanced on measured confounders.22 Survival by SNH designation was compared using Cox proportional hazards models with inverse probability treatment weights. The weights were estimated using a multinomial regression model; the dependent variable was SNH category (non-SNH, l-SNH, or h-SNH), and the predictor variables were year of diagnosis, patient demographics, poverty index, tumor characteristics, and treatment provision. Sensitivity analysis did not appreciably change the direction, magnitude, or significance of the hazards ratios (data not shown); therefore, we report results of the primary analysis only.

Because a portion of hospitals changed safety net designation over time, we conducted a sensitivity analysis to evaluate the impact of change in safety net designation on overall survival. We performed a Cox proportional hazards model, similar to above, among hospitals that maintained the same safety net status for the entire study period. An alternative analysis using safety net designation as a time-varying covariate was not possible because the TCR does not specify the amount of time a patient spent at a specific hospital.

All statistical tests were 2-sided, and the significance level was $P = .05$. All statistical analyses were performed using STATA version 14 (StataCorp, College Station, TX).

This study was approved by the Texas Department of State Health Services and the Institutional Review Board at the University of Texas Southwestern Medical Center.

RESULTS

Hospital and Patient Population
A total of 328 acute short-term hospitals were included in this analysis: 254 (77%) non-SNHs, 49 (15%) l-SNHs, and 25 (8%) h-SNHs. During the study period, SNHs (l-SNHs and h-SNHs) cared for 42% of HCC patients (n = 7432). The proportion of HCC patients treated in SNHs increased from 41% (n = 779) in 2001-2002 to 44% (n = 1750) in 2011-2012. Table 1 lists hospital characteristics according to safety net designation. SNHs were larger hospitals; h-SNH had a median of 200 beds compared with 70 beds at non-SNHs ($P = .03$), and the volume of HCC patients (defined as the number of HCC patients managed at a hospital) was significantly higher at SNHs (median annual HCC volume: 3 and 6 patients annually at l-SNHs and h-SNHs, respectively, vs 2 patients annually at non-SNHs; $P = .04$). A higher proportion of l-SNHs and h-SNHs were teaching institutions compared with non-SNHs (39% and 40%, respectively, vs 17%; $P < .01$ for both comparisons). Oncology services including palliative care and radiology resources (eg, imaging and image-guided radiation capabilities) were similar across all 3 hospital types.

There were 15,932 patients with HCC exclusively receiving care at non-SNHs or SNHs: 10,066 (63%) patients received care at non-SNHs, 4149 (26%) received care at l-SNHs, and 1717 (11%) received care at h-SNHs. Across all hospital types, the number of newly diagnosed HCC patients nearly doubled over the study period (Table 2). The majority patients treated at SNHs were Hispanic (51% and 71% at l-SNHs and h-SNH, respectively, vs 26% at non-SNHs; $P < .01$ for both comparisons). Over half of HCC patients treated at l-SNHs and 73% of HCC patients treated at h-SNHs lived in the highest poverty category. In contrast, most patients at non-SNHs were non-Hispanic white (57%), and less than a third resided in the highest poverty category. A higher proportion of patients at non-SNHs had private insurance compared with l-SNHs and h-SNHs (17% vs 9% and 3%, respectively; $P < .01$ for both comparisons).
TABLE 2. Characteristics of 15,932 Patients Diagnosed With Incident HCC by Hospital Safety Net Designation, 2001-2012

| Characteristics           | Non-SNH (n = 10,066) | l-SNH (n = 4149) | h-SNH (n = 1717) | P     |
|---------------------------|----------------------|-----------------|-----------------|-------|
| Year of diagnosis         |                      |                 |                 | <.01  |
| 2001-2004                 | 2404 (24)            | 965 (23)        | 460 (27)        |       |
| 2005-2008                 | 3344 (33)            | 1280 (31)       | 508 (30)        |       |
| 2009-2012                 | 4318 (43)            | 1904 (46)       | 749 (44)        |       |
| Age, y                    |                      |                 |                 | <.01  |
| 18-54                     | 2515 (25)            | 1287 (31)       | 432 (25)        |       |
| 55-64                     | 3003 (30)            | 1412 (34)       | 476 (28)        |       |
| >75                       | 2349 (23)            | 813 (20)        | 352 (21)        |       |
| Sex                       |                      |                 |                 | <.01  |
| Female                    | 2911 (29)            | 1007 (24)       | 475 (28)        |       |
| Male                      | 7155 (71)            | 3142 (76)       | 1242 (72)       |       |
| Race/Ethnicity            |                      |                 |                 | <.01  |
| White                     | 5699 (57)            | 1192 (29)       | 252 (15)        |       |
| African-American          | 1272 (13)            | 626 (15)        | 193 (11)        |       |
| Hispanic                  | 2573 (26)            | 2120 (51)       | 1219 (71)       |       |
| Asian                     | 486 (5)              | 203 (5)         | 52 (3)          |       |
| Poverty index             |                      |                 |                 | <.01  |
| <5%                       | 1409 (14)            | 292 (7)         | 42 (3)          |       |
| <10%                      | 1974 (20)            | 448 (11)        | 113 (7)         |       |
| <20%                      | 3383 (34)            | 1087 (26)       | 299 (18)        |       |
| >20%                      | 3142 (32)            | 2292 (58)       | 1216 (73)       |       |
| Type of insurance         |                      |                 |                 | <.01  |
| None                      | 326 (3)              | 451 (11)        | 88 (5)          |       |
| Private                   | 1671 (17)            | 394 (9)         | 53 (3)          |       |
| Medicaid                  | 520 (5)              | 357 (9)         | 158 (9)         |       |
| Medicare                  | 2786 (28)            | 967 (23)        | 389 (22)        |       |
| Military                  | 277 (3)              | 64 (2)          | 31 (2)          |       |
| Missing                   | 4486 (45)            | 1916 (46)       | 998 (58)        |       |
| Tumor stage               |                      |                 |                 | <.01  |
| Localized                 | 4066 (40)            | 1814 (44)       | 625 (36)        |       |
| Regional                  | 1685 (17)            | 720 (17)        | 297 (17)        |       |
| Metastatic                | 1865 (19)            | 809 (20)        | 373 (22)        |       |
| Not reported              | 2450 (24)            | 806 (19)        | 422 (22)        |       |

Abbreviations: HCC, hepatocellular carcinoma; h-SNH, high-proportion safety net hospital; l-SNH, low-proportion safety net hospital; non-SNH, non-safety net hospital.

**Treatment Use**

Tumor stage was similar between patients at SNHs and non-SNHs, but there were differences in treatment receipt by hospital categories (Table 3). Although treatment use was similar between non-SNHs and l-SNHs (45% vs 45%; P = .72; adjusted odds ratio [OR], 0.97; 95% confidence interval [CI], 0.89-1.06), it was significantly lower at h-SNHs (32%; OR, 0.64; 95% CI, 0.57-0.73) compared with non-SNH. This pattern was consistent across stage of disease. Approximately 60% of patients with localized disease at both non-SNHs and l-SNHs received HCC-directed treatment, whereas only 40% of patients with localized disease at h-SNHs underwent HCC-directed treatment (P < .01). Compared with non-SNH patients, patients with localized HCC were more likely to undergo curative treatment at l-SNHs (31% vs 35%; P < .01; OR, 1.30; 95% CI, 1.14-1.49) but less likely to do so at h-SNHs (31% vs 15%; P < .01; OR, 0.51; 95% CI, 0.40-0.66). Among patients with regional HCC, a higher proportion of patients at non-SNHs received curative therapies compared with patients at l-SNHs and h-SNHs (14% vs 12% and 5%, respectively; P < .01 for both comparisons) as well as chemotherapy (40% vs 32% and 33%, respectively; P < .01 for both). Similarly, among patients with metastatic HCC, a higher proportion of patients received chemotherapy in non-SNHs (33%) than l-SNHs (27%) and h-SNHs (24%; P < .01). Among patients surviving more than 2 months (conditional landmark analysis), treatment receipt (overall and stage-specific) was similar by safety net designation (data not shown).

**Overall Survival**

Overall survival differed by safety net designation (Fig. 1). Compared with patients at non-SNHs, overall survival was higher in patients at l-SNHs (median survival, 6.8 vs 5.5 months; P < .01; OR, 1.30; 95% CI, 1.14-1.49). Among patients with regional HCC, overall survival differed by safety net designation (Fig. 2). Compared with non-SNHs, overall survival was higher in patients at l-SNHs (median survival, 5.2 vs 4.5 months; P < .01; OR, 1.30; 95% CI, 1.14-1.49). Among patients with metastatic HCC, overall survival was higher in patients at l-SNHs (median survival, 3.8 vs 3.1 months; P < .01; OR, 1.30; 95% CI, 1.14-1.49).
5.9 months; \( P = .04 \); adjusted hazard ratio (HR), 0.93; 95% CI, 0.89-0.98) (Table 4) but significantly worse at h-SNHs (median survival, 3.0 vs 5.9 months; HR, 1.30; 95% CI, 1.22-1.39; \( P < .01 \)). A similar conclusion was noted when the survival analysis was conducted among hospitals that maintained the same safety net designation over the entire study period (non-SNHs vs h-SNHs: HR, 1.25; 95% CI, 1.14-1.37) (see Supporting Information). Moreover, similar survival patterns were observed in subgroup analyses of patients with localized (non-SNH 12.7 months, I-SNH 14.7 months, and h-SNH 5.1 months) (Fig. 2A) and regional HCC (5.1 months, 4.9 months, and 3.3 months, respectively) (Fig. 2B). On multivariable analysis, differences in survival for localized HCC remained significant after adjusting for year of diagnosis, patient demographics (age, sex, and race), poverty index, and treatment (I-SNHs vs non-SNHs: HR, 0.91; 95% CI, 0.84-0.98; I-SNHs vs non-SNHs: HR, 1.53; 95% CI, 1.38-1.71). Similar patterns were observed for patients with regional disease: care at I-SNHs was associated with marginally better survival compared with non-SNHs (I-SNHs vs non-SNHs: HR, 0.91; 95% CI, 0.81-1.01; h-SNHs vs non-SNHs: HR, 1.19; 95% CI, 1.03-1.37). In patients with metastatic disease, overall survival was consistently poor across all hospital categories (median survival, 2.1-2.6 months) (Fig. 2C). Notably, there was no evidence of concerning multicollinearity among the predictor variables in the survival model, and interaction terms were not statistically significant (Table 4). Evaluation of overall survival between treated and untreated patients with nonmetastatic disease demonstrated a consistent pattern of lowest survival at h-SNHs. The difference in mortality risk (between h-SNHs and non-SNHs), however, was attenuated with addition of treatment to the survival model (without treatment: HR, 1.53; 95% CI, 1.41-1.66; with treatment: HR, 1.40; 95% CI, 1.29-1.53). Overall and stage-specific survival by safety net designation were similar in the conditional landmark analysis among patients surviving more than 2 months, without notable changes in the direction or significance of the HR estimated in the unconditional survival analysis.

**DISCUSSION**

to the best of our knowledge, we have conducted the first population-based study comparing presentation, treatment, and survival among HCC patients treated in SNHs and non-SNHs. Using a comprehensive state cancer model...
registry in the state with the highest incidence of HCC in the United States,\textsuperscript{3} we found that SNHs disproportionately care for racial/ethnic minorities and socioeconomically disadvantaged HCC patients. HCC patients at h-SNHs were significantly less likely to undergo HCC-directed treatment despite similar tumor stage at diagnosis, and among those with localized HCC, fewer patients at h-SNHs received curative treatment. Differences in care delivery between SNHs and non-SNHs likely contributed to worse overall and stage-specific survival among patients treated at SNHs.

Although several studies have highlighted racial/ethnic disparities in HCC incidence and prognosis, few have characterized the relative contribution of biological and health care delivery factors to these disparities.\textsuperscript{1,6,23,24} Our comparison of hospitals in Texas suggests that health care delivery factors, specifically differences in treatment delivery, play an important role in HCC disparities. If confirmed in future studies, these data highlight a potential intervention target to reduce racial/ethnic disparities and socioeconomic disparities in HCC prognosis.

Differences in treatment delivery between SNHs and non-SNHs are likely driven by a combination of system-, provider-, and patient-level factors. Our study shows that SNHs and non-SNHs have comparable liver transplantation, oncology, and radiology resources, although we did not obtain data regarding other factors, including clinic and operating room capacity, patient panel size, and degree of nursing support, which may vary among health systems. At the provider level, SNHs suffer from limited availability of specialty services at SNHs and difficulty accessing off-site specialty care for uninsured patients.\textsuperscript{25} In addition, providers at SNHs likely have different levels of knowledge about HCC surveillance and treatment compared with those at non-SNHs. Potential HCC knowledge gaps among providers may include misconceptions about screening and treatment guidelines for HCC.\textsuperscript{26–29} At the patient level, individuals at SNHs often undergo less preventive care, have advanced medical comorbidity, and have notable nonmedical social barriers to care.\textsuperscript{10,30,31} Previous studies have also suggested differential levels of knowledge about HCC between SNHs and non-SNHs.\textsuperscript{32,33} Although we did not find differences in treatment and overall survival by safety net designation in a conditional landmark analysis accounting for patient comorbidity and liver function, these findings highlight the importance of large multicenter studies using clinically granular data to explore reasons for differences in treatment and outcomes between SNHs and non-SNHs.

Our study has some limitations. First, we used administrative data lacking information on liver function, performance status, and comorbidity. Although we attempted to account for this limitation using conditional landmark analysis, unmeasured confounding from these
factors could have biased our results, because previous studies have suggested that HCC patients at safety net systems may have worse liver function compared with those seen at tertiary care centers. Second, tumor stage was categorized by SEER instead of more clinically relevant HCC staging systems such as the Barcelona Clinic Liver Cancer staging system. This lack of granularity may potentially explain similarities in tumor stage between SNHs and non-SNHs, and non-SNHs may still have higher use of HCC surveillance and early tumor detection than SNHs. Third, treatment data in the cancer registry reflect only the first course of treatment; treatment of recurrent or progressive disease as well as treatment delivered following an initial bridging therapy were not available. Furthermore, around 8% of patients were missing treatment information; however, the pattern of missingness was similar across safety net categories. Fourth, chemotherapy in TCR does not distinguish between chemoembolization and systemic chemotherapy despite differences in eligible patient populations and prognosis. Last, our results rely on the completeness and accuracy of the information recorded in the TCR database.

In conclusion, our study revealed suboptimal treatment utilization, despite similar tumor stage at diagnosis, and worse overall and stage-adjusted survival among patients treated at SNHs. Amid national health care reform, and as the number of patients with HCC continues to increase, a better understanding of the differences in care delivery between SNHs and non-SNHs is a crucial step toward informing reform strategies and guiding resource allocation with the aim of reducing cancer care disparities.

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