Predictors of Surgical Intervention for Hepatocellular Carcinoma

Race, Socioeconomic Status, and Hospital Type

Yulia Zak, MD; Kim F. Rhoads, MD, MS, MPH; Brendan C. Visser, MD

Objectives: To define current use of surgical therapies for hepatocellular carcinoma (HCC) and evaluate the correlation of various patient and hospital characteristics with the receipt of these interventions.

Design: Retrospective cohort.

Setting: California Cancer Registry data linked to the Office of Statewide Health Planning and Development patient discharge abstracts between 1996 and 2006.

Patients: Patients with primary HCC.

Main Outcome Measures: Receipt of liver transplant, hepatic resection, or local ablation.

Results: Of 12,148 HCC cases, 2,390 (20%) underwent surgical intervention. Three hundred eleven (2.56%) received a liver transplant, 1,307 (10.8%) underwent resection, and 772 (6.35%) had local ablation. There were wide variations in treatment by race and hospital type. African American and Hispanic patients were less likely than white patients to undergo transplant ($P < .05$). African American and Hispanic patients were less likely than white and Asian/Pacific Islander patients to have hepatectomy or ablation ($P < .05$). In multivariable analysis, the apparent differences in surgical intervention by race/ethnicity were decreased when adjusting for the patients’ socioeconomic and insurance statuses. Patients with lower socioeconomic status and no private insurance were less likely to receive any surgery ($P < .01$). Hospital characteristics also explained some variations. Disproportionate Share Hospitals and public, rural, and nonteaching hospitals were less likely to offer surgical treatment ($P < .01$).

Conclusion: There are significant racial, socioeconomic, and hospital-type disparities in surgical treatment of HCC.
Variation in the use of surgical interventions for HCC has previously been documented in the literature. Investigators have shown differences in the incidence and the receipt of therapy by certain racial and ethnic groups, as well as by geographic location. Some have correlated differences in the use of surgery to poor survival for these populations. Thus far, however, to our knowledge, none have assessed the association between the individual socioeconomic level, insurance status, or hospital characteristics with variations in care. It is also unknown whether there is any variation in the use of local ablative therapy in patients with HCC.

To define the current use of various surgical interventions for HCC, we performed a retrospective cohort study to demonstrate the association of individual patient factors and hospital characteristics with the use of surgical interventions. The hypothesis is that the use of surgical interventions varies by individual patient characteristics, including race/ethnicity, socioeconomic status (SES), and insurance status and, furthermore, is correlated with certain hospital characteristics.

**METHODS**

**SOURCES OF DATA**

For the purposes of the current study, California Cancer Registry (CCR) data were linked to the California Office of Statewide Health Planning and Development (OSHPD) patient discharge abstracts. This data set was subsequently linked to hospital characteristics from the publicly available California Hospital Annual Financial Data File (HAFD).

The CCR contains data collected via a statewide cancer-reporting program mandated by the California Health and Safety Code (sections 103875-103885) and managed by the California Department of Health Services in collaboration with the Public Health Institute and 8 regional cancer registries. California state law requires that all hospitals, physicians, and certain other health care providers report every clinical encounter where cancer is the primary diagnosis regardless of treatment administered during the encounter. All relevant clinical, radiologic, or pathologic data, with the exception of those associated with nonmelanoma skin cancer and carcinoma in situ of the cervix, are reported. This decreases the loss-to-follow-up rate for patients who complete treatment within the state, even if primary and secondary treatments are administered in separate hospitals. The registry contains fewer than 3% missing race data and fewer than 3% of records obtained from death certificates. In addition to detailed information about the individual tumors, with grade, stage, and select molecular marker data, the database also contains census block group–level sociodemographic data, including a validated composite SES score that accounts for employment, median income, and education level.

The California OSHPD patient discharge database collects data for all discharges from more than 400 general, acute, nonfederal hospitals in the state. In addition to the principal diagnosis (reason for admission) and the principal procedure, coded using the International Classification of Diseases, Ninth Revision, Clinical Modification, the database also contains coding for up to 24 additional diagnoses (secondary diagnoses) and up to 19 additional procedures performed during the index hospitalization. California has 1 of only 2 databases nationwide to historically require all secondary diagnoses be entered with comitant coding for whether the condition was present on admission. Condition present on admission coding allows for distinction between comorbidities and hospital-acquired conditions (ie, complications) and therefore facilitates risk adjustment of outcomes in multivariable models. The database also contains demographic information including age at diagnosis, sex, and insurance status. Hospital volume can be derived based on the total number of discharges for a particular diagnosis aggregated at the hospital level.

Data from the CCR are linked to OSHPD data using a probabilistic linkage method employing day, month, and year of birth in conjunction with the patient’s social security number. The linkage was performed by the staff at the CCR, stripped of identifying linking variables before disclosure to the investigators. Office of Statewide Health Planning and Development–assigned unique hospital identifiers were then used to link the CCR-OSHPD data to HAFD. The HAFD contain hospital-level characteristics such as geographic location; Disproportionate Share status (Disproportionate Share Hospital [DSH]); hospital ownership; and teaching hospital status as designated by the state. The study was approved by the California Committee for the Protection of Human Subjects, the CCR, and the Stanford University institutional review board.

**STUDY COHORT**

All patients admitted with the diagnosis of primary HCC (principal diagnosis code 155.0) to California general, acute, nonfederal hospitals between 1996 and 2006 were identified in the linked database described earlier. One hundred one patients with unknown sex or those in the racial category Alaskan native/American Indian were excluded because of cell size, in accordance with the data user agreements. Those with a secondary diagnosis of HCC were not included in the analysis.

**DATA ANALYSIS**

Analyses were performed using SAS 9.1 for Windows (SAS Institute Inc, Cary, North Carolina). Bivariate comparisons were conducted using $\chi^2$ to define HCC management and demonstrate associations between the different types of surgical interventions (liver resection vs transplant vs ablation) as related to patient characteristics (age, sex, race, SES, insurance status, Charlson comorbidity scores), as well as according to hospital characteristics (disproportionate share of uncompensated care hospitals [DSHs], private vs public, rural vs urban, and teaching vs nonteaching institutions). Because some of the patient characteristics can affect the current distribution of disease interventions, multivariable logistic regression analysis was used to calculate adjusted odds ratios (ORs) predicting the use of surgical procedures as a function of patient factors and hospital characteristics. Multivariable models were constructed using forward selection methods. A forward selection criterion for model fit of $P = .20$ was used. The ORs and 93% confidence intervals (95% CIs) were estimated for each covariate in the model. All tests of significance were 2-tailed. Statistical significance was defined as an OR not equal to 1, a 95% CI that does not cross 1, and a $P$ value <.05.

The primary outcome under study was receipt of surgical intervention. The secondary outcome was the subtype of intervention received. Patients with International Classification of Diseases, Ninth Revision, Clinical Modification procedure codes corresponding to liver resection (50.0, 50.2, 50.22, 50.29, 50.3, and 50.9), transplant (50.5, 50.51, and 50.59), or local ablation (50.23, 50.24, 50.25, and 50.26) were coded as having undergone the named procedure. Those lacking codes for any of
these procedures were treated as having undergone no surgical intervention.

Patient-level predictor variables included age, race/ethnicity, and sex. Type of insurance and individual socioeconomics were also included in the multivariable models. Severity of comorbid illness was defined using the Deyo et al modified Charlson Index\(^{18,19}\) for each individual patient. Hospital characteristics evaluated for the study included annual HCC volume; teaching status; rural or nonrural location; public vs private hospital ownership; and DSH status. While volume was calculated based on number of records listing HCC as the primary diagnosis on an average annual basis, all other variables were defined in the HAFD for 2001. The CCR and OSHPD discharge data span 1996 through 2006; therefore, HAFD for 2001 (the middlemost point between the 2 extremes) were used to define hospital characteristics.

### RESULTS

A total of 12,480 HCC cases were recorded in California from 1996 to 2006. Twenty percent of these patients underwent surgical therapy, with 311 liver transplants (2.56%), 1307 hepatic resections (10.8%), and 772 radiofrequency ablations (6.35%) performed as part of their treatment. Eighty percent of patients received no surgical intervention. **Table 1** details our analysis of surgical interventions for HCC as a function of patient demographic variables and hospital characteristics.

The majority of patients in the cohort were 45 to 74 years of age. Patients older than 75 years were less likely to undergo a surgical procedure than all younger patients.
patients, who had similar rates of surgical intervention. These differences persisted for each individual intervention, with $P < .01$ for all comparisons.

There were more men than women in the cohort: 8668 (71%) vs 3480 (29%); however, there were no significant differences in the use of surgical treatment by sex. Twelve percent of women vs 10.2% of men underwent hepatic resection ($P = .29$), 2.5% of women and 2.6% of men received a liver transplant ($P = .18$), and 6.9% of women vs 6.1% of men received local ablation ($P = .88$).

**SURGICAL INTERVENTION AND PATIENT FACTORS**

There were significant differences in the distribution of surgical treatments by race. Twenty-one percent of white patients, 14% of African American patients, 16% of Hispanic patients, and 22% of Asian/Pacific Islander patients received some type of surgical intervention. African American and Hispanic patients were significantly less likely to undergo transplant ($P < .01$), resection ($P < .01$), or ablation ($P < .05$) than white or Asian groups.

As the number of comorbid diseases increased, there was a decrease in the proportion of patients undergoing any surgical procedure ($P < .01$). However, there was no difference in surgical modality between groups with different Charlson comorbidity scores ($P = .19$ for transplant, $P = .09$ for resection, and $P = .08$ for ablation).

Patients with lower SES were less likely to receive any surgical intervention ($P < .01$). The proportion of transplants in the highest socioeconomic quintile was 4 times that of the lowest quintile, and patients within the highest SES cohort were twice as likely to undergo liver resection than those in the lowest quintile. These differences, however, did not reach statistical significance ($P = .39$ for transplant and $P = .11$ for resection). A significant difference in liver ablation was noted between the groups ($P = .05$).

Insurance status was also associated with surgical intervention ($P < .01$). There were significant differences in the use of transplant ($P < .01$) and local ablation ($P < .01$), but not liver resection ($P = .11$), across groups. A 3-fold higher percentage of patients with private insurance underwent liver resection as compared with those with no insurance.

### Table 2: Multivariable Logistic Regression Baseline Model 1 Estimating the Odds of Different Racial Groups Getting Surgical Intervention for HCC in California Hospitals, 1996 to 2006, After Adjustment for the Effect of Patient Demographics

<table>
<thead>
<tr>
<th>Race</th>
<th>Any Surgical Procedure</th>
<th>Transplant</th>
<th>Resection</th>
<th>Ablation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR Estimate (95% CI)</td>
<td>$P$ Value</td>
<td>OR Estimate (95% CI)</td>
<td>$P$ Value</td>
</tr>
<tr>
<td>African American vs white</td>
<td>0.59 (0.48-0.72)</td>
<td>&lt; .01</td>
<td>0.42 (0.23-0.77)</td>
<td>.02</td>
</tr>
<tr>
<td>Hispanic vs white</td>
<td>0.67 (0.59-0.76)</td>
<td>&lt; .01</td>
<td>0.8 (0.60-1.10)</td>
<td>.37</td>
</tr>
<tr>
<td>Asian/Pacific Islander vs</td>
<td>1.26 (1.17-1.37)</td>
<td>&lt; .01</td>
<td>0.79 (0.60-1.04)</td>
<td>.39</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; HCC, hepatocellular carcinoma; OR, odds ratio.

*Model adjusts for age and sex. Odds ratios not equal to 1 are considered statistically significant if the 95% CI excludes 1 and the $P$ value is < .05.

### SURGICAL INTERVENTION AND PATIENT FACTORS: MULTIVARIABLE ANALYSIS

Table 2 shows the odds of surgery and each of the surgical modalities by race. These models were adjusted for patient demographic and clinical characteristics (sex, age, race, and comorbidity score). This reveals that African American patients were less likely to receive any surgery ($P < .01$) and were 58%, 36%, and 24% less likely to undergo transplant ($P < .01$), resection ($P < .05$), and ablation ($P < .03$), respectively. Hispanic patients were less likely to receive any surgical intervention ($P < .01$), which was largely accounted for by the 48% decrease in receipt of hepatectomy ($P < .01$). When comparing Hispanic populations with white, there were no differences noted for transplant or ablation. In sharp contrast, Asian populations were more likely to undergo surgical intervention ($P < .01$) and this phenomenon was most pronounced in resection (OR, 1.36; $P < .01$) and ablation (OR, 1.18; $P < .01$).

Table 3 shows racial and ethnic differences in treatment when the baseline demographic models were further adjusted for SES and insurance status. With this modification, the apparent differences in surgical intervention by race/ethnicity were decreased. The disparity in receipt of “any surgery” persisted for African American patients; however, the OR of undergoing transplant increased from 0.42 (95% CI, 0.23-0.77) to 0.54 (95% CI, 0.30-0.99), and the odds of having ablation increased from 0.76 (95% CI, 0.60-0.97) to 0.83 (95% CI, 0.59-1.17). The odds of resection increased from 0.64 (95% CI, 0.50-0.83) to 0.77 (95% CI, 0.60-1.00), making the difference between African American and white patients nonsignificant with $P = .28$. For Hispanic patients, the disparity in undergoing “any surgery” was eliminated after adjustment for SES and insurance status. The OR of receiving a transplant increased to 1.3 (95% CI, 1.02-1.65) as compared with white patients. The odds of resection improved from 0.52 (95% CI, 0.44-0.62) to 0.63 (95% CI, 0.53-0.76), although this was still significantly less than the odds of white patients undergoing liver resection, with $P < .01$. The odds of ablation for Hispanic patients increased from 0.98 (95% CI, 0.81-1.20) to 1.13 (95% CI, 0.92-1.39) and remained at $P > .05$. The disparity in all surgical interventions together between Asian and white patients persisted with adjustment for SES/insurance category, but the difference in the rates of ablation de-
creased to become nonsignificant (P = .07). Therefore, some of the disparity seen initially in our bivariate comparisons and the baseline multivariable regression analysis seems to be related to the differences in the groups’ SES and insurance status.

Adjustment for hospital characteristics in the baseline model of patient demographics did not significantly affect or explain the differences in care noted by race (data not shown).

**SURGICAL INTERVENTION AND HOSPITAL CHARACTERISTICS**

Significant variation in the provision of surgical therapies was noted in comparing teaching and nonteaching hospitals (P < .01 for all surgery types). Most of the liver transplants took place at teaching hospitals (P < .01). Teaching institutions also proved to be 1.5 times more likely to resect liver tumors and almost 3 times more likely to administer local ablative therapy (Table 1). Non-DSHs were more likely to provide surgical intervention (P < .01). Specifically, 3% of non-DSHs vs 1% of DSHs offered transplant (P < .01), and 7% of non-DSHs vs 6% of DSHs provided ablation (P < .01). There was no difference in the rate of liver resections among these institutions (P = .14). Private institutions tended to offer more resections (12% vs 4%; P < .01) and transplants (3% vs 0%; P < .01), but not local ablations (P = .28), than public hospitals. There were no significant differences in any surgical interventions between rural and urban centers in univariable analyses.

In multivariable models predicting the odds of surgery and each of the surgical modalities by hospital characteristic, while adjusting for patient sex, age, race, and comorbidity score, all institutional variations in the type of attempted curative therapy persisted (Table 4). Significant differences appeared between rural and urban institutions in any surgical interventions and liver resections in particular (P < .01). Adjusting for SES/insurance type also did not affect the treatment variations based on hospital characteristics.

The results of the current study show that only a small proportion of patients with HCC in California undergo surgical intervention. The data paint a picture of a typical patient receiving surgical therapy for HCC in California as more likely to be younger, be of higher SES, have private insurance, be white or Asian/Pacific Islander, and have fewer comorbid conditions. These patients receive their care at private, teaching, non-DSH institutions.

**COMMENT**

The broad variation in delivery of surgical intervention may result from a lack of rigorous and convincing evidence about the relative efficacy of potentially curative treatments for the disease. This may be further exacerbated by the numerous staging schemata, most of which fail to accurately predict who will do well with each treatment modality. These factors have made it difficult to establish clear clinical guidelines for the treatment of this serious disease. Despite the clinical factors driving

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**Table 3. Multivariable Logistic Regression Model 2 Demonstrating the Effect of Socioeconomic Status and Insurance Category on the Odds of Getting Surgical Intervention for Different Racial Groups**

<table>
<thead>
<tr>
<th>Race</th>
<th>Any Surgical Procedure</th>
<th>Transplant</th>
<th>Resection</th>
<th>Ablation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR Estimate (95% CI)</td>
<td>P Value</td>
<td>OR Estimate (95% CI)</td>
<td>P Value</td>
</tr>
<tr>
<td>African American vs white</td>
<td>0.75 (0.61-0.93)</td>
<td>&lt; .01</td>
<td>0.54 (0.30-0.99)</td>
<td>.05</td>
</tr>
<tr>
<td>Hispanic vs white</td>
<td>0.94 (0.85-1.04)</td>
<td>.21</td>
<td>1.3 (1.02-1.65)</td>
<td>.04</td>
</tr>
<tr>
<td>Asian/Pacific Islander vs</td>
<td>1.19 (1.09-1.29)</td>
<td>&lt; .01</td>
<td>0.83 (0.63-1.09)</td>
<td>.95</td>
</tr>
<tr>
<td>white</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; OR, odds ratio.

*Model adjusts for patient demographics (age and sex), socioeconomic status, and insurance category. Odds ratios not equal to 1 are considered statistically significant if the 95% CI excludes 1 and the P value is < .05.

**Table 4. Multivariable Logistic Regression Model 2 Demonstrating the Effect of Various Hospital Characteristics on the Odds of Getting Surgical Intervention**

<table>
<thead>
<tr>
<th>Hospital Characteristic</th>
<th>Any Surgical Procedure</th>
<th>Transplant</th>
<th>Resection</th>
<th>Ablation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR Estimate (95% CI)</td>
<td>P Value</td>
<td>OR Estimate (95% CI)</td>
<td>P Value</td>
</tr>
<tr>
<td>Teaching vs nonteaching</td>
<td>3.16 (2.86-3.49)</td>
<td>&lt; .01</td>
<td>15.11 (10.51-21.72)</td>
<td>&lt; .01</td>
</tr>
<tr>
<td>Non-DSH vs DSH</td>
<td>1.96 (1.75-2.22)</td>
<td>&lt; .01</td>
<td>4.76 (3.46-6.67)</td>
<td>&lt; .01</td>
</tr>
<tr>
<td>Rural vs urban</td>
<td>12.5 (3.03-50)</td>
<td>&lt; .01</td>
<td>b</td>
<td>b</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; DSH, Disproportionate Share Hospital; OR, odds ratio.

*Model adjusts for patient demographics (age and sex) and hospital type. Odds ratios not equal to 1 are considered statistically significant if the 95% CI excludes 1 and the P value is < .05.

*Cell size too small to calculate reliable estimates.
variation in care, the explanations for disparities are not completely clear.

There are prior studies that have shown that African American patients do not receive the same cancer-related therapies as white patients, several in particular address variations in the receipt of liver transplants among African American, white, and Asian/Pacific Islander patients. The current study confirms the presence of racial disparities in all surgical interventions for HCC. In addition, this is the first investigation, to our knowledge, that addresses disparities in the distribution of all 3 available surgical interventions (transplant, resection, and local ablation) across the 4 large racial/ethnic patient populations with consideration of the effect of socioeconomic factors and insurance category.

The explanatory strength of SES suggests that differences in access to appropriate health care may be responsible for the differences in management of HCC. Previous research has shown that African American patients with HCC are more likely to have an annual household income less than $25,000 and less likely to have Medicare and private health insurance. In addition, Guidry et al found that African American individuals tended to reach their insurance spending limits more frequently than white individuals and were more likely to lose medical insurance coverage after being diagnosed with cancer. These are all factors that may limit minorities’ access to the most suitable surgical treatment for HCC.

Not all of the racial disparity is due to the differences in SES and health insurance status in our data, however. Differences in underlying comorbidities may also contribute to the apparent disparity in treatment. For example, hepatitis C virus–related HCC is higher among African American patients (53.7%) as compared with white (51.7%) and Asian (29.9%) patients. This means that the prevalence of hepatitis C virus–related cirrhosis is also higher in African American patients, potentially leading to fewer recommendations of surgical therapy for HCC by health care professionals. Rates of alcoholic cirrhosis are also higher in the African American population, which may delay liver transplants for otherwise appropriate candidates. There is some evidence that African American patients may present with more advanced disease, thus, fewer African American patients may have disease that is actually appropriate for surgical intervention. Nevertheless, while there are a number of factors that may contribute to the racial disparities seen in the management of HCC, it does appear that the bulk are related to the differences in the groups’ socioeconomic standing and health insurance category.

The second major finding of this study is that there are marked variations in the management of HCC among different hospitals, with private, teaching, non-DSH institutions more likely to provide surgical intervention. There is previous research showing that hospitals with a high proportion of Medicaid patients are less likely to achieve a high-performance status and that different geographic regions provide varying levels of surgical care for patients of different races/ethnicities. In our data, however, although there were independent variations in treatment among different hospitals, racial and ethnic disparities in the receipt of appropriate care were explained more by SES and insurance status than by location of care. The reason for this may be that the distribution of the patient population with varying socioeconomic levels and health insurance statuses within any given hospital is so wide that it masks the measurable effects of the hospital category on the received treatment.

The methods in this study allowed us to circumvent some of the limitations of prior investigations in this field. Many previous investigations of HCC treatment patterns are limited in that they used the National Cancer Institute Surveillance, Epidemiology, and End Results database, which includes only specific geographic regions and limited sociodemographic data, or the Medicare data, which only track patients beyond the age of 65 years (and would, according to our data, exclude 64% of patients receiving surgical treatment for HCC). These analyses often also do not separate out Hispanic Americans from the other racial groups and do not allow one to examine other factors that may affect the approach to patient treatment, such as patient SES, expected source of payment, or the type of admitting hospital. In this analysis, the use of CCR allowed for the inclusion of the entire population of this large, diverse state. This allowed for accurate analysis of cancer treatment as a function of demographic, geographical, and socioeconomic factors within a large population that is representative of the United States. Linking these data to the financial and use data from the individual hospitals, found in the OSHPD, permitted its correlation with additional hospital-specific variables.

However, there are limitations to this study that are inherent in the source of our data. The nature of a retrospective analysis of secondary data limits the ability to attribute causality. There are also no data to determine whether and/or how the type of delivered care affects patient survival. In addition, CCR and OSHPD do not provide accurate data regarding the stage of HCC at the time of the recorded surgical intervention. If a large proportion of patients had more advanced HCC and/or concomitant liver disease at the time of diagnosis, this may partially explain why only 20% of the patients received any type of surgical treatment. Given prior reports showing that African American patients present with more advanced disease at the time of diagnosis, and develop HCC at a younger age, it is possible that minorities also present to public non-teaching DSHs with more diffuse disease more often than nonminorities. In these cases, underuse of tumor resection, transplant, and local ablation may be justified.

In conclusion, our study demonstrates variations in care based on minority status, socioeconomic class, insurance category, and hospital financial and academic profiles. This underscores the importance of health disparity research in the area of hepatocellular carcinoma and identifies a clear need to more closely examine and modify the impact of these variations on patient outcomes.

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REFERENCES


ONLINE FIRST
The Golden State of Healthcare Reform

Ethnoeconomic Origins of Outcome Imbalance

The tragedy of population-based registry studies is that they are defined by their limitations. The tools are cumbersome, the numbers are immense, and it is easy to get lost in Leviathan logistics, misattributing significance and underinterpreting covariable confounders. By avoiding microdissection, Zak and colleagues have elegantly displayed the snapshot, landscape overview that underpins the strengths of database analysis. This unique perspective suggests socioeconomic and ethnic inequity in HCC treatment in California. Surprised? This registry is known to have ethnic misclassification and, as in all databases, other inaccuracies are likely. Disaggregating socioeconomic data by census block group level makes crude assumptions based on common denominator assignment. As Zak and colleagues attest, this study is further limited by the lack of disease stage and