DOI:10.1111/hpb.12427

#### **ORIGINAL ARTICLE**

# Disparities in care for patients with curable hepatocellular carcinoma

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#### **Abstract**

**Background:** The incidence of hepatocellular carcinoma (HCC) is increasing, but surgical management continues to be underutilized. This retrospective review investigates treatment decisions and survival for early stage HCC.

**Methods:** The National Cancer Database (NCDB) was queried for all patients with curable HCC (Stage I/II) from 1998 to 2011 (n = 43~859). Patient and tumour characteristics were analysed to determine predictors of having surgery and of long-term survival.

**Results:** Only 39.7% of patients received surgery for early stage HCC. Surgical therapies included resection (34.6%), transplant (28.7%), radiofrequency ablation (27.1%) and other therapies. Surgery correlated with improved median survival (48.3 versus 8.4 months), but was only performed on 42% of stage I patients and 50% of tumours smaller than 2 cm. Patients were more likely to receive surgery if they were Asian or white race, had private insurance, higher income, better education, or treatment at an academic centre (P < 0.05). However, private insurance and treatment at an academic centre were the only variables associated with improved survival (P < 0.05).

**Conclusion:** Fewer than half of patients with curable HCC receive surgery, possibly as a result of multiple socioeconomic variables. Past these barriers to care, survival is related to adequate and reliable treatment. Further efforts should address these disparities in treatment decisions.

Received 11 March 2015; accepted 13 April 2015

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#### Introduction

Hepatocellular carcinoma (HCC) is the fifth most common solid organ tumour and the third leading cause of cancer-related death worldwide.<sup>1</sup> The incidence of HCC has been increasing for years, but incidence-based mortality has slowed, probably owing to earlier detection and intervention.<sup>2</sup> However, there is a large population of patients with curable disease who do not receive surgical management. A recent meta-analysis found an average rate of curative intent surgery of 22%, ranging from 14 to 51%.<sup>3</sup> Rates were higher in single-centre studies, and the rate for early stage HCC was 59%. Rates of

This study was presented at the Annual Meeting of the AHPBA, 11-15 March 2015, Miami, Florida.

surgical management in other studies range from 20 to 57%.<sup>4–7</sup> While the phenomenon of underutilized surgical care is known, the reasons for this disparity remain unclear.

The present study aims to provide a comprehensive understanding of surgical management for early stage HCC. This analysis utilized a nationally validated, prospectively gathered, cancer database to investigate how many patients with potentially curable disease receive surgical management and what variables are associated with treatment decisions and survival.

#### **Patients and methods**

#### Data source

Data for this study were drawn from the American College of Surgeons National Cancer Data Base (NCDB) liver Participant User File (PUF) for the years 1998–2011. This is a nationwide, 748 **HPB** 

facility-based, clinical data set that captures 70% of all diagnosed malignancies in the US.<sup>8</sup> The NCDB collects de-identified patient-level data from nationally accredited cancer programme registries using standardized data items and coding definitions. These data include patient demographics as well as detailed information regarding cancer staging, tumour histology, treatment types and courses, short-term surgical outcomes, and long-term survival.

#### **Patient cohort**

The liver PUF was queried for all patients with clinical stage I/II HCC (n = 43~859), according to the AJCC Cancer Staging Manual edition in use during the year in which the case was diagnosed. Subtypes of HCC were excluded. Patients were separated into groups who did and did not receive surgical management, defined as surgical resection, liver transplant, radiofrequency ablation and other liver-directed therapies. The following patient information was collected for all patients: age (years), gender, race (Asian, black, white or other), primary insurance, income (median household income for patient zip code based on 2000 US Census data, in quartiles), education (median percentage of adults in the patient's zip code without a high school degree [HSD] based on 2000 US Census data, in quartiles), tumour grade, tumour size (<2 cm, 2–5 cm, >5 cm), AJCC clinical stage (I or II), patient Charlson/Deyo comorbidity score (0,1,2), facility type (academic: > 500 new cancer diagnoses annually, at least four postgraduate training programmes; comprehensive community: >500 new cancer diagnoses annually, postgraduate training optional; community: 100-500 new cancer diagnoses annually, postgraduate training optional; and other), Urban/ Rural status (metropolitan, urban, rural), great circle distance (distance in miles between patient's residence and reporting hospital), surgical procedure (resection, transplant, radiofrequency ablation, other/unknown) for patients who had surgery and AJCC pathological stage (I–IV) for patients who had surgery.

#### Statistical analysis

The two cohorts were compared with respect to the variables above using chi-squared tests for categorical variables and rank-sum tests for continuous variables. Kaplan-Meier survival analysis was used to compare survival between the two groups. For survival analyses, data were limited to the years 1998-2006 to ensure appropriate follow-up. As a result of this and limitations based on missing data, only 15 235 patients (10.2%) were included in the survival analysis. Multiple logistic regression models were created to analyse predictors of having surgery and 30-day mortality; Cox regression was used to model longterm survival. The following variables of clinical interest were included in the models: clinical stage, age, gender, race, primary insurance, income, education, Charlson-Deyo score and facility type. An alpha level of 0.05 was used for all significance tests. The data were analysed using SAS 9.3 (SAS Institute, Cary, NC, USA).

#### **Results**

#### Patient, tumour and facility characteristics

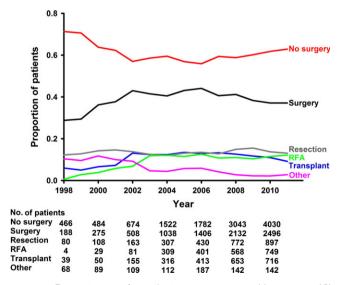
Table S1 (available online as Supporting Information) describes the cohorts of patients who did and did not receive surgical management for the stage I/II HCC. Overall, not quite 40% of patients received surgical management. The rates of surgical management over time in this cohort are presented in Fig. 1. Patients who received surgery were younger, less likely to be black and more often privately insured. Income and education were directly correlated with increasing rates of surgical management.

Surgical therapy was more common for smaller tumours. However, tumours graded as 'moderately differentiated' were most likely to receive surgery. Post-operatively, only 5.9% of tumours were upstaged to stage III or IV, and none were downstaged to stage 0. Also of note, patients with a Charlson—Deyo score of 0 were less often managed surgically.

Surgical therapy was much more common in academic centres than community centres. There was little variation based on urban/rural designation, but patients who ended up having surgery travelled further for their care than patients who did not

#### Predictors of surgery and post-operative mortality

Results from the multivariate analysis for predictors of receiving surgical management are in Table 1. Asian patients were more likely than whites to receive surgery, and black patients were less likely. Lower odds of surgery were associated with clinical stage II versus I, increasing age and male gender. Also less likely to have surgery were patients without private insurance, with low income, with less education and those not treated at academic centres.



**Figure 1** Percentage of patients per year with stage I/II hepatocellular carcinoma (HCC) who have surgical management. RFA, radiofrequency ablation

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