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Surgical Therapy for Early Hepatocellular Carcinoma in the Modern Era:

A 10-Year SEER-Medicare Analysis

Hari Nathan, MD, PhD, Omar Hyder, MD, Skye C. Mayo, MD, MPH, Kenzo Hirose, MD, Christopher L. Wolfgang, MD, PhD, Michael A. Choti, MD, and Timothy M. Pawlik, MD, MPH, PhD

Department of Surgery, Johns Hopkins University School of Medicine, Baltimore, MD

Abstract

Objective—We sought to quantify the use of and analyze factors predictive of receipt of surgical therapy for early hepatocellular carcinoma (HCC).

Background—The incidence of HCC is increasing, and the options for surgical therapy for early HCC have expanded, but the use of surgical therapy for early HCC has not been examined in a modern cohort.

Methods—A retrospective cohort study was performed using data from the 1998–2007 Surveillance, Epidemiology, and End Results-Medicare linked database. Data were analyzed for patients 66 years of age and older with early HCC (tumors ≤ 5 cm without metastatic disease, nodal metastasis, extrahepatic extension, or major vascular invasion). Both Surveillance, Epidemiology, and End Results and Medicare data were used to ascertain receipt of therapy as well as comorbidity burden and other patient and hospital variables. Multivariable logistic regression models were used to analyze factors associated with receipt of therapy.

Results—Our selection criteria identified 1745 patients for this study. Most patients had tumors between 2 and 5 cm in size (n = 1440, 83%). Solitary tumors (n = 1121, 64%) were more common than multiple tumors (n = 624, 36%). A total of 820 patients (47%) with early HCC received no surgical therapy. Among 741 patients with solitary, unilobar tumors and microscopic confirmation of HCC, 246 (33%) received no surgical therapy. Of 535 patients with no liver-related comorbidities, 273 (51%) did not receive surgical therapy. In multivariable analysis, patient age, income, tumor factors, liver-related comorbidities, and hospital factors were associated with receipt of surgical therapy.

Conclusions—Although some patients with early HCC may not be candidates for surgical therapy, these data suggest that there is a significant missed opportunity to improve survival of patients with early HCC through the use of surgical therapy.

Keywords

hepatocellular carcinoma; SEER-Medicare; surgery; therapy

Although it has historically been a cancer of the developing world, the incidence of hepatocellular carcinoma (HCC) is rising in the United States¹ and other developed countries,² both as the result of chronic hepatitis C and perhaps as a result of the increasing prevalence of the metabolic syndrome.³ The prognosis of HCC has historically been poor: although it is the sixth most common cancer, it is the third leading cause of cancer death worldwide.⁴ Surgical therapy represents the only opportunity for cure, and advances in surgical therapy for HCC over the last 2 decades have expanded the range of surgical options available to these patients. Most commonly, these include liver ablation (LA), liver resection (LR), and liver transplantation (LT), all of which can achieve acceptable survival outcomes in selected patients^{5–10} and all of which are being used with greater frequency for HCC.¹¹

Previous studies have examined patterns of therapy for HCC.^{12,13} El-Serag et al¹² analyzed data on patients with HCC diagnosed between 1992 and 1999 and found that 13% of patients received surgical therapy. Shah et al¹³ analyzed data on patients with HCC diagnosed between 1991 and 2005 and found that 30% of patients received some type of therapy and 14% received surgical therapy. Both studies included patients from the early 1990s, which preceded widespread acceptance of LT for HCC,⁵ the advent of parenchyma-sparing LR for HCC,¹⁴ and improvements in surgical mortality after LR.¹⁵ In addition, both studies included patients with a wide spectrum of HCC disease burden.

We sought to assess the use of surgical therapy in patients with early HCC, that is, those patients with nonmetastatic tumors 5 cm or smaller and without evidence of nodal disease, extrahepatic extension of tumor, or major vascular invasion. Ostensibly, these patients are both the most amenable to and most likely to benefit from appropriate surgical therapy. Because of recent advances in the surgical treatment of HCC, we focused on a modern era in HCC management. Specifically, we sought to quantify the use of LA, LR, and LT in patients with early HCC, assess liver-specific and other comorbidities that might preclude surgical therapy, and analyze factors predictive of receipt of surgical therapy for early HCC. As a secondary goal, we also sought to examine the use of nonsurgical therapy for early HCC. We used the Surveillance, Epidemiology, and End Results (SEER)-Medicare linked database for this analysis.

METHODS

A retrospective cohort study was performed using data from the SEER-Medicare linked database for the years 1998–2007. The characteristics and representativeness of this database have been discussed previously.¹⁶ Patients aged 66 years and older with at least 1 year of continuous non-health maintenance organization Medicare part A and part B enrollment before diagnosis were selected to allow for appropriate identification of medical comorbidities. Younger patients were excluded to avoid including a disproportionate number of patients meeting criteria for Medicare eligibility other than age, such as end-stage

renal disease. Those patients with a diagnosis of HCC (*International Classification of Diseases for Oncology, Third Edition*,¹⁷ histology codes 8170 to 8175 for HCC and site code C22.0 for liver) were selected for this study. SEER histology codes may or may not be based on a tissue diagnosis, but the presence or absence of microscopic confirmation is reported by SEER and was included as a variable for analysis. Patients diagnosed at autopsy or by death certificate were excluded. Patients with another malignant primary tumor diagnosed within 5 years before their HCC diagnosis were excluded to minimize the chance that metastatic disease to the liver was misdiagnosed as HCC. Because the focus of this analysis was on early HCC, patients with metastatic disease, tumors larger than 5 cm, nodal metastasis, extrahepatic extension, or invasion of branches of the portal or hepatic veins or extrahepatic vessels were excluded, as were patients with missing data for any of these elements.⁸

Patient demographic and tumor variables were ascertained from SEER data. Median income was used as a surrogate for socioeconomic status, with a preference for census tract median income if available, followed by ZIP code median income, census tract per capita income, and ZIP code per capita income.¹⁸ Receipt of first surgical therapy (LA, LR, or LT) was primarily determined from SEER data. If SEER identified a surgical procedure, this was considered to be the first surgical therapy regardless of Medicare data. If SEER did not identify surgical therapy but Medicare data did, then the first surgical therapy was assigned using Medicare data. Medicare data were also used to ascertain use of nonsurgical therapy—transcatheter arterial (chemo) embolization (TACE/TAE), portal vein embolization, or chemotherapy—and subsequent courses of therapy after the initial surgical therapy. Linkage to hospital data was based on the hospital at which initial therapy was received or, if no therapy was received, at the first hospital where the patient was admitted after diagnosis of HCC.

Patient comorbidities were ascertained using both inpatient and outpatient Medicare claims¹⁹ for a window 1 year before to 3 months after HCC diagnosis using the comorbidity index proposed by Elixhauser et al²⁰ and the composite Elixhauser comorbidity score proposed by van Walraven et al²¹ In addition, *International Classification of Diseases, Ninth Revision (ICD-9)* diagnosis codes that could indicate liver disease were individually tabulated: chronic hepatitis C (70.41, 70.44, 70.51, 70.54, 70.70, 70.71), chronic hepatitis B (70.22, 70.23, 70.32, 70.33), other viral hepatitis (70.52, 70.53, 70.59, 70.6, 70.9), nonviral hepatitis (571.40, 571.41, 571.42, 571.49, 573.3), alcoholic liver disease (571.0, 571.1, 571.2, 571.3), nonalcoholic cirrhosis (571.5, 571.6, 571.8, 571.9), portal hypertension [572.3, also including ascites (789.5x), esophageal varices (456.0, 456.1, 456.2x), and hepatorenal syndrome (572.4)], coagulopathy (286.7), and hepatic encephalopathy/coma (70.4x, 70.6, 572.2). These were constructed so as to be maximally inclusive of conditions that might preclude surgical therapy for HCC and thus avoid underestimating the number of patients who may have had liver-related contraindications to certain surgical therapies.

All counts 1 to 10 are reported as “<11” in accordance with SEER-Medicare confidentiality requirements. Bivariate comparisons were performed using Fisher exact test, the rank sum test, or Cuzick’s nonparametric test for trend,²² as appropriate. Multivariable logistic regression was performed to model the receipt of surgical therapy, yielding odds ratios

(OR). Similarly, a multinomial logistic regression model was used to model the choice between different types of surgical therapy (LA, LR, or LT), yielding relative risk ratios (RRR). In both cases, robust standard errors were calculated to account for clustering by health service area. Survival statistics were tabulated using the Kaplan-Meier method,²³ and comparisons of survival between groups were performed using the log-rank test. Variables with $P < 0.1$ in bivariate analysis were initially entered into the model, and the model was refined using Akaike information criteria.²⁴ All tests of statistical significance were 2-sided, and statistical significance was established at $P < 0.05$. Statistical analyses were performed using Stata/MP 10.1 for Windows (StataCorp LP, College Station, TX). This study was deemed exempt from review by the Johns Hopkins University School of Medicine Institutional Review Boards.

RESULTS

Our selection criteria identified 1745 patients with early HCC diagnosed between 1998 and 2007 (Table 1). The majority of patients were aged 65 to 74 years ($n = 1030$, 59%), with the remainder aged 75 years and older. Most patients were male (63%), and most were white (64%), but a significant minority were Asian/Pacific Islander (28%). The vast majority (93%) lived in urban areas. There was an increase in the annual number of cases included in the cohort over the years of the study from 94 (5%) in 1998–1999 to 600 (34%) in 2006–2007.

Comorbidities were assessed using the Elixhauser index. The median number of comorbidities was 5, and the median composite comorbidity score was 15. Specific liver-related comorbidities were also tabulated. Viral hepatitis was present in 772 patients (44%) and nonviral hepatitis in 506 (29%). Alcoholic liver disease was present in 288 patients (17%) and nonalcoholic cirrhosis in 1041 (60%). Based on codes for portal hypertension, ascites, esophageal varices, and hepatorenal syndrome, 455 patients (26%) had some degree of portal hypertension. Finally, 41 patients had coagulopathy (2%) and 196 patients (11%) had hepatic encephalopathy.

With respect to tumor characteristics, the median tumor size was 3.4 cm in this cohort that was selected for tumor size 5 cm or smaller. Most patients had tumors between 2 and 5 cm in size ($n = 1440$, 83%). Solitary tumors ($n = 1121$, 64%) were more common than multiple tumors ($n = 624$, 36%). There was evidence of bilobar disease in 311 patients (18%). There was microscopic confirmation of HCC in 1319 patients (76%). Data on α -fetoprotein levels were available for 839 patients diagnosed in 2004 or later. α -Fetoprotein levels were reported as “positive/elevated” in 581 patients (69%), “negative/normal” in 254 patients (30%), and “borderline” in fewer than 11 patients.

There was good agreement between SEER and Medicare data regarding the first course of surgical therapy (Table 2). Of the 916 cases originally classified by SEER as having received no surgical therapy, 105 were reclassified as having had surgery on the basis of Medicare data. A small number of patients (<11) with missing data on surgical therapy from SEER but no surgical Medicare claims were reclassified as having received no surgical therapy. As a result, based on a conservative estimate from combined SEER-Medicare data,

a total of 820 patients (47%) with early HCC received no surgical therapy. Overall, LA was the most common surgical modality ($n = 527$, 30%), followed by LR ($n = 280$, 16%) and LT ($n = 118$, 7%). The distribution of surgical therapies did not vary over the period of the study ($P = 0.3$, Fig. 1). The reason that surgical therapy was not performed was ascertained from SEER data for the 820 patients who did not receive surgical therapy. In 622 cases (76%), surgery was not recommended. In 65 cases (8%), surgery was contraindicated because of other conditions. Surgery was recommended but not performed because of patient refusal ($n = 22$, 3%), patient death ($n < 11$), or unknown reasons ($n = 99$, 12%) in the remaining 124 cases.

Medicare claims were also used to ascertain receipt of nonsurgical therapies. Of the 820 patients receiving no surgical therapy, 59 (7%) underwent TACE/TAE, 12 (1%) portal vein embolization, and 127 (15%) systemic chemotherapy. The remaining 622 patients (76% of those receiving no surgical therapy and 36% of the total cohort) had no evidence of any therapy for HCC found in either SEER or Medicare data.

Receipt of therapy was examined in specific subgroups that would potentially have the best oncologic outcomes or carry the least perioperative risk. There were 176 patients with solitary, unilobar HCC smaller than 2 cm. Among these patients, no surgical therapy was performed in 58 (33%), and 49 (28%) had no evidence of therapy at all in SEER or Medicare data. To assess the possibility that some of these tumors were thought to be dysplastic nodules and not true HCC, thus justifying ongoing surveillance instead of surgical therapy, we examined the 741 patients with solitary, unilobar tumors and microscopic confirmation of HCC. Of these 741 patients, 246 (33%) received no surgical therapy, and 186 (25%) received no therapy at all. When we further restricted the cohort to the 122 patients with solitary, unilobar tumors smaller than 2 cm but still with microscopic confirmation of HCC, 27 (22%) received no surgical therapy and 24 (20%) received no therapy at all. When we analyzed data on the 62 patients with solitary, unilobar tumors smaller than 2 cm and elevated α -fetoprotein levels, 16 (26%) received no surgical therapy and 13 (21%) received no therapy at all. There were 450 patients in the lowest quartile of the composite Elixhauser comorbidity score (median score, 0). Of these patients, no surgical therapy was performed in 221 (49%), and 201 (47%) received no therapy at all. There were 535 patients with none of the liver-related comorbidities described in Table 1, 273 (51%) of whom did not receive surgical therapy and 248 (46%) of whom did not receive any therapy at all. A very small number of patients ($n = 43$) had both highly favorable tumor characteristics and no liver-related comorbidities, but in this small group 15 patients (35%) did not receive surgical therapy.

Factors associated with receipt of surgical therapy were examined in bivariate analyses (Table 3). Patient age, race, and income were all associated with receipt of surgical therapy. Surgical patients were younger, more often Asian/Pacific Islander, and lived in areas with higher median incomes. Comorbidity profiles were similar overall, but there were differences in specific liver-related comorbidities. Viral hepatitis was more common in the surgical group than the non-surgical group (49% vs 39%, $P < 0.001$) as was nonviral hepatitis (34% vs 24%, $P < 0.001$). Alcoholic liver disease was slightly more common in the nonsurgical group (19% vs 14%, $P = 0.005$), and nonalcoholic cirrhosis was more common

in the surgical group. Evidence of portal hypertension was present in 29% of the nonsurgical group and 23% of the surgical group ($P = 0.003$). With respect to tumor characteristics, patients who received surgical therapy generally had smaller tumors (median 3.1 cm vs 3.5 cm, $P < 0.001$), more often had solitary tumors (68% vs 60%, $P < 0.001$), and less often had bilobar disease (14% vs 22%, $P < 0.001$).

The hospitals where patients were initially treated were identified for 1216 patients. Most patients were treated at teaching hospitals ($n = 952$, 78%) and urban hospitals ($n = 766$, 63%). With respect to cancer treatment, 468 (38%) of the patients' treating hospitals were American College of Surgeons Oncology Group (ACOSOG) participants, 21 (2%) were National Cancer Institute (NCI) cancer centers, and 224 (18%) were NCI comprehensive cancer centers. The NCI cancer center designations were combined for further analysis. In bivariate analysis, teaching hospital status, ACOSOG status, and NCI status were associated with receipt of surgical therapy (Table 3).

A multivariable logistic regression model was used to examine independent factors associated with receipt of surgical therapy (Table 4). The initial model included patient data only due to the large amount of missing hospital data. Younger patient age and higher income were associated with receipt of surgical therapy. Patients with nonviral hepatitis (OR, 1.53, $P < 0.001$) or nonalcoholic cirrhosis (OR, 1.47, $P = 0.001$) were more likely to receive surgical therapy, whereas those with alcoholic liver disease (OR, 0.62, $P < 0.001$) or portal hypertension (OR, 0.57, $P = 0.001$) were less likely to receive surgical therapy. Patients with bilobar disease were similarly less likely to receive surgical therapy (OR, 0.57, $P < 0.001$).

Hospital factors were then added to this multivariable model and tested for significance. In the model including all 4 hospital variables that we studied, associations of patient factors were all similar to those shown in Table 4. In addition, receipt of surgical therapy was associated with treatment at a teaching hospital [OR: 2.22, 95% confidence interval (CI): 1.45–3.42, $P < 0.001$], urban hospital (OR: 1.51, 95% CI: 1.12–2.03, $P = 0.007$), ACOSOG hospital (OR: 1.76, 95% CI: 1.20–2.57, $P = 0.004$), or NCI cancer center (OR: 2.31, 95% CI: 1.68–3.17, $P < 0.001$).

A multinomial logistic regression model was used to model the decision between LA, LR, and LT. Patients with portal hypertension were more likely to receive LT over LA (RRR: 3.78, 95% CI: 2.13–6.70) and LT over LR (RRR: 7.58, 95% CI: 3.36–17.1) ($P < 0.001$ for variable overall). Patients with nonviral hepatitis were more likely to receive LR over LA (RRR: 1.49, 95% CI: 1.11–2.01) and LR over LT (RRR: 1.57, 95% CI: 0.99–2.49) ($P = 0.02$ for variable overall). The presence of nonalcoholic cirrhosis was associated with a trend toward increased use of LA over LR (RRR: 1.28, 95% CI: 0.95–1.74) and LA over LT (RRR: 1.70, 95% CI: 0.79–3.67) ($P = 0.02$ for variable overall). Patients with multifocal tumors were more likely to receive LT over LA (RRR: 1.94, 95% CI: 1.25–3.02) and LT over LR (RRR: 2.90, 95% CI: 1.82–4.63) ($P < 0.001$ for variable overall). Tumors larger than 2 cm were more likely to be treated with LR over LT (RRR: 1.97, 95% CI: 1.13–3.44, $P = 0.05$ for variable overall).

Survival varied by receipt of therapy. Median survival from date of diagnosis was 11 months for patients receiving no surgical therapy, 27 months for LA, 40 months for LR, and 104 months for LT ($P < 0.001$). A similar pattern was observed for 1-year survival (no surgery 46%, LA 79%, LR 78%, and LT 89%) and 5-year survival (no surgery 7%, LA 20%, LR 33%, LT 63%) ($P < 0.001$). In the group with solitary, unilobar HCC smaller than 2 cm, 5-year survival was slightly better than in the early HCC group as a whole (no surgery 14%, LA 29%, LR 52%, LT 54%, $P < 0.001$).

DISCUSSION

Although HCC often carries a poor prognosis, detection at an early stage offers the promise of improved survival,²⁵ but realization of this potential requires the application of appropriate therapy. The incidence of HCC is rising in the United States,^{1,2} and surgical therapy for HCC is being applied with more frequency.¹¹ Our primary objective was to assess the use of potentially curative surgical therapy in patients with early HCC, who are most likely to be candidates for and most likely to benefit from LA, LR, or LT. Overall, 47% of these highly selected patients did not receive surgical therapy. Several even more favorable subgroups were examined, and the proportion of patients not receiving surgical therapy was consistently 20% to 30%. As expected, patients receiving surgical therapy had better survival than those not receiving surgical therapy.

Several predictors of receipt of surgical therapy were identified. Older patient age and lower income were associated with less receipt of surgical therapy, a finding that has been previously reported in broader cohorts of patients with HCC.^{12,13,26} We also quantified the impact of tumor-related factors such as tumor size (even in a cohort that had tumors ≤ 5 cm) and multilobar involvement. Not surprisingly, patients with larger tumor and multilobar involvement were less likely to receive surgical therapy. Finally, although a composite comorbidity score was not associated with receipt of surgical therapy, specific liver-related comorbidities were. Alcoholic liver disease and portal hypertension were associated with lower utilization of surgical therapy. When surgical therapy was performed, patients with portal hypertension were more likely to receive LT than LA or LR. The presence of nonviral hepatitis was associated with increased receipt of surgical therapy, mainly LR. Patients with nonalcoholic cirrhosis were also more likely to receive surgical therapy. Although data were limited, we also found that receipt of surgical therapy was increased at teaching hospitals, urban hospitals, ACOSOG hospitals, and NCI cancer centers.

There are several advantages to using the linked SEER-Medicare data for this study with respect to providing a fair assessment of the use of surgery in patients with early HCC. First, using the combination of SEER data and Medicare claims improves identification of cancer-directed surgery over either data source alone.²⁷ Second, we were able to assess comorbidity burden, which can be a contraindication to major cancer-directed surgery. We maximized sensitivity for comorbidities by using both part A and part B Medicare data¹⁹ and by using the Elixhauser comorbidity algorithm.²⁸ In particular, liver-related comorbidities such as decompensated cirrhosis can preclude certain surgical options, but we were able to examine specific subgroups of patients, including those without documented liver-related comorbidities.

Our study has several important limitations. Our patient cohort only included patients aged 66 years and older, which limits generalizability to younger patients. Previous data indicate that the median age of patients with early HCC is 63 years,⁸ so this study is directly applicable to roughly half the adult population with early HCC. Second, this study's applicability is also limited to the United States; the findings might change in countries with different health care financing systems and organ transplantation policies. Third, we did attempt to use physician claims data to assess whether patients with early HCC were evaluated by various specialists, such as gastroenterologists, surgeons, and medical oncologists. However, a large amount of missing data precluded such an analysis in this study. We have previously shown that the type of specialist that a patient visits influences the recommendation of surgical therapy for HCC.²⁹ We theorize that the physician's attitude toward and advocacy for particular surgical therapies for HCC likely influence ultimate receipt of surgical therapy.

In conclusion, in a Medicare population of patients with early HCC in the modern era, only one half of patients received surgical therapy. Receipt of surgical therapy was influenced by demographic factors, tumor size and distribution, liver-related comorbidities, and hospital factors. Although some patients with early HCC may not be candidates for surgical therapy, these data suggest that there is a significant missed opportunity to improve survival of patients with early HCC through the use of surgical therapy. All patients with early HCC should be evaluated for surgical therapy to ensure that recent therapeutic advances for HCC are being applied in all appropriate cases. We suggest that increased referral of patients with HCC to centers with substantial liver surgery experience may ameliorate this problem.

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FIGURE 1.

Receipt of surgical therapy over time: (A) number of cases and (B) proportion of cases. $P = 0.3$ for trend over time.

TABLE 1

Patient and Tumor Characteristics (N = 1745)

Variable	Number	%
Age, y		
65–69	513	29
70–74	517	30
75–79	421	24
80–84	207	12
85–89	87	5
Sex		
Male	1091	63
Female	654	37
Race		
White	1119	64
Asian/Pacific Islander	497	28
Black	112	6
American Indian/Alaskan/Unknown	17	<1
Urban or rural		
Urban	1629	93
Rural	116	7
Income quartile		
1	437	25
2	436	25
3	437	25
4	435	25
Year of diagnosis		
1998–1999	94	5
2000–2001	190	11
2002–2003	355	20
2004–2005	506	29
2006–2007	600	34
Elixhauser comorbidities		
Number (median, IQR)	5	2–7
Score (median, IQR)	15	0–24
Liver-related comorbidities		
Chronic hepatitis C	650	37
Chronic hepatitis B	215	12
Other viral hepatitis	88	5
Any viral hepatitis (HCV, HBV, other)	772	44
Non-viral hepatitis	506	29
Alcoholic liver disease	288	17
Nonalcoholic cirrhosis	1041	60

Variable	Number	%
Portal hypertension	455	26
Coagulopathy	41	2
Hepatic encephalopathy	196	11
Tumor size (all 5 cm)		
Size in cm (median, IQR)	3.4	2.5–4.1
Size >2 cm	1440	83
Multifocality		
No	1121	64
Yes	624	36
Bilobar		
No	1293	74
Yes	311	18
Unknown	141	8

IQR indicates interquartile range; HBV, hepatitis B virus; HCV, hepatitis C virus.

TABLE 2

First Surgical Therapy: Agreement of SEER and Medicare Data

Medicare First Surgical Therapy	SEER First Surgical Therapy				Missing	Total
	None	LA	LR	LT		
None	811	145	53	22	<11	1040
LA	95	276	11	<11	<11	392
LR	<11	<11	212	<11	<11	227
LT	<11	<11	<11	76	<11	86
Total	916	431	277	110	11	1745

SEER indicates Surveillance, Epidemiology, and End Results.
Cell counts less than 11 have been suppressed per SEER-Medicare confidentiality rules.

TABLE 3

Factors Associated With Receipt of Surgical Therapy

Variable	Surgical Therapy		<i>P</i>
	No	Yes	
Number of patients	820	925	
Age, y			
65–69	24%	34%	<0.001
70–74	28%	31%	
75–79	27%	22%	
80–84	14%	10%	
85–89	8%	2%	
Sex			
Male	61%	64%	0.2
Female	39%	36%	
Race			
White	67%	62%	0.045
Asian/Pacific Islander	25%	31%	
Black	7%	6%	
American Indian/Alaskan/Unknown	1%	1%	
Urban or rural			
Urban	94%	93%	0.2
Rural	6%	7%	
Income quartile			
1	28%	22%	<0.001
2	26%	24%	
3	24%	26%	
4	22%	27%	
Year of diagnosis			
1998–1999	6%	4%	0.2
2000–2001	11%	11%	
2002–2003	22%	19%	
2004–2005	27%	31%	
2006–2007	34%	35%	
Elixhauser comorbidities			
Number (median)	5	5	0.3
Score (median)	15	14	
Liver-related comorbidities			
Chronic hepatitis C	32%	42%	<0.001
Chronic hepatitis B	10%	14%	0.006
Other viral hepatitis	5%	5%	0.9
Any viral hepatitis (HCV, HBV, other)	39%	49%	<0.001
Non-viral hepatitis	24%	34%	<0.001

Variable	Surgical Therapy		
	No	Yes	P
Alcoholic liver disease	19%	14%	0.005
Non-alcoholic cirrhosis	56%	63%	0.005
Portal hypertension	29%	23%	0.003
Coagulopathy	2%	2%	0.8
Hepatic encephalopathy	13%	10%	0.1
Tumor size (all < 5 cm)			
Size in cm (median)	3.5	3.1	<0.001
Size >2 cm	85%	80%	0.005
Multifocality			
No	60%	68%	<0.001
Yes	40%	32%	
Bilobar			
No	67%	80%	<0.001
Yes	22%	14%	
Unknown	10%	6%	
Hospital characteristics*			
Teaching hospital	66%	87%	<0.001
Urban hospital	60%	65%	0.09
ACOSOG hospital	27%	47%	<0.001
NCI cancer center	10%	28%	<0.001

* Data available for 1216 patients.

ACOSOG indicates American College of Surgeons Oncology Group; HBV, hepatitis B virus; HCV, hepatitis C virus; NCI, National Cancer Institute.

TABLE 4

Multivariable Logistic Regression: Receipt of Surgical Therapy

Variable	OR	95% CI	P
Age, y			
65–69	Reference		<0.001
70–74	0.69	0.52–0.90	
75–79	0.53	0.37–0.75	
80–84	0.49	0.34–0.72	
85–89	0.20	0.12–0.32	
Income quartile			
1	Reference		0.04
2	1.14	0.85–1.54	
3	1.34	1.06–1.70	
4	1.53	1.06–2.22	
Liver-related comorbidities			
Nonviral hepatitis	1.53	1.25–1.87	<0.001
Alcoholic liver disease	0.62	0.47–0.80	<0.001
Non–alcoholic cirrhosis	1.47	1.18–1.83	0.001
Portal hypertension	0.57	0.41–0.79	0.001
Tumor size (all ≥ 5 cm)			
Size ≤ 2 cm	Reference		0.03
Size >2 cm	0.75	0.58–0.97	
Multifocality			
No	Reference		0.09
Yes	0.80	0.62–1.04	
Bilobar			
No	Reference		<0.001
Yes	0.57	0.42–0.78	
Unknown	0.48	0.33–0.70	

CI indicates confidence interval; OR, odds ratio.