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Healthcare Costs Related to Treatment of Hepatocellular Carcinoma Among Veterans With Cirrhosis in the United States

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Abstract

BACKGROUND & AIMS—It is important to quantify medical costs associated with hepatocellular carcinoma (HCC), the incidence of which is rapidly increasing in the United States, for development of rational healthcare policies related to liver cancer surveillance and treatment of chronic liver disease. We aimed to comprehensively quantify healthcare costs for HCC among patients with cirrhosis in an integrated health system and develop a model for predicting costs that is based on clinically relevant variables.

METHODS—Three years subsequent to liver cancer diagnosis, costs accrued by patients included in the Veteran's Outcome and Cost Associated with Liver disease cohort were compiled by using

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Supplementary Material

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Conflicts of interest

The authors disclose no conflicts.

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the Department of Veterans Affairs Corporate Data Warehouse. The cohort includes all patients with HCC diagnosed in 2008–2010 within the VA with 100% chart confirmation as well as chart abstraction of tumor and clinical characteristics. Cancer cases were matched 1:4 with non-cancer cirrhosis controls on the basis of severity of liver disease, age, and comorbidities to estimate background cirrhosis-related costs. Univariable and multivariable generalized linear models were developed and used to predict cancer-related overall cost, survival, and cost per life-year.

RESULTS—Our analysis included 3188 cases of HCC and 12,722 controls. The mean 3-year total cost of care in HCC patients was $154,688 (standard error, $150,953–$158,422) compared with $69,010 (standard error, $67,344–$70,675) in matched cirrhotic controls, yielding an incremental cost of $85,679; 64.9% of this value reflected increased inpatient costs. In univariable analyses, receipt of transplantation, Barcelona Clinic Liver Cancer (BCLC) stage, liver disease etiology, hospital academic affiliation, use of multidisciplinary tumor board, and identification through surveillance were associated with cancer-related costs. Multivariable generalized linear models incorporating transplantation status, BCLC stage, and multidisciplinary tumor board presentation accurately predicted liver cancer–related costs (Hosmer-Lemeshow goodness of fit; *P* value ≅ 1.0).

CONCLUSIONS—In a model developed to comprehensively quantify healthcare costs for HCC among patients with cirrhosis in an integrated health system, we associated receipt of liver transplantation, BCLC stage, and multidisciplinary tumor board with higher costs but increased survival time. Models that predict total costs on the basis of receipt of liver transplantation were constructed and can be used to model cost-effectiveness of therapies focused on HCC prevention.

Keywords

Cirrhosis; Hepatocellular Carcinoma; Child-Turcotte-Pugh Score; Hepatitis; Human; Liver; Survival; Natural History; Database; Transplant

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Hepatocellular carcinoma (HCC) incidence and mortality in the United States continue to increase; it is the fifth and ninth leading cause of cancer death in men and women, respectively.[1] Therapeutic options used for HCC, including liver resection, liver transplantation, ablative therapies, transarterial embolotherapy/radiotherapy, systemic therapy, and palliative care, are associated with widely ranging and often profound costs. Accurate estimates of HCC-related costs are critically needed to understand the societal burden of chronic liver disease as well as to evaluate the cost-effectiveness of interventions designed to reduce HCC incidence and/or promote early diagnosis. For instance, cost-effectiveness analyses related to high-cost antiviral regimens for chronic hepatitis C are dependent on accurate estimates of the costs of hepatic complications prevented through cure.[2,3] Similarly, the cost-effectiveness of HCC surveillance programs is partially predicated on the differential costs of cancers identified earlier by surveillance.[4,5]

Estimates of 3- to 10-year total costs for HCC care have ranged widely from $12,683[6] to $176,456[7] largely on the basis of the interventions available to the study population.[6–12] Several important limitations of these previous analyses include (1) utilization of the Surveillance Epidemiology and End Results (SEER)-Medicare registry[8,12] that contains limited clinical data on mainly elderly patients who are less likely to receive recommended

treatments[13] and who are often not considered candidates for high-cost interventions such as liver transplantation[13,14]; (2) utilization of cost data predating the introduction of systemic and radiotherapy therapy for HCC[6,8,9,11]; (3) incomplete capture of transplantrelated costs[9]; (4) limitation of analysis to patients with viral hepatitis[7,9,12]; and/or (5) biases related to selection from a liver transplantation waitlist population.[7] A unique feature of HCC is its close association with cirrhosis, a condition with significant and partially independent costs[9,15] that often dictates the nature of safe and effective treatment modalities.[16] Liver cancer progression generally hastens death through liver failure rather than through complications of metastatic disease, possibly shifting costs toward inpatient management of complications such as ascites, encephalopathy, and variceal bleeding as opposed to progressively intense outpatient systemic therapies. Few studies have analyzed the impact of cirrhosis severity or cancer stage at presentation on subsequent HCC-related costs.[7]

The Veterans Affairs (VA) medical system is the largest integrated provider of liver-related healthcare in the United States, caring for more than 60,000 patients with cirrhosis and more than 2000 incident cases of HCC annually since 2010.[17] Although predominantly male, veterans with HCC in the VA represent both non-elderly and elderly patients with a wide range of liver disease etiologies cared for in urban, suburban, and rural care settings.[18] Comprehensive clinical, pharmacy, laboratory, radiology, and procedural data, and costs associated therewith, performed within the VA or paid by VA funds are administratively accessible. In this study, our objective was to quantify absolute per-patient costs of HCC care as well as the relative cost of HCC above costs associated with underlying cirrhosis stratified by liver disease severity, liver cancer stage, receipt of HCC surveillance, and receipt of liver transplantation.

Methods

Patients and Data Sources

National data from the VA Corporate Data Warehouse for all patients with 2 outpatient or 1 inpatient International Classification of Disease-CM, version 9 (ICD9-CM) codes for cirrhosis (571.2, 571.5, 571.6) from January 1, 2008 to December 31, 2010 were obtained under Institutional Review Board-approved protocols.[19] Demographic data, inpatient and outpatient ICD9-CM codes, Common Procedural Terminology (CPT) codes, and pharmacy and laboratory data from January 1, 2002 to December 31, 2012 were obtained. Death was ascertained by using the Vital Status File (censoring as of December 31, 2012).[20] Liver transplantation status was obtained from Organ Procurement and Transplantation Network STAR-file data.[21]

HCC cases were selected on the basis of an initial HCC diagnosis (2 outpatient or 1 inpatient ICD9-CM codes: 155.0, 155.2 excluding 155.1)[22] and 100% verified by chart extraction.[18] Extractors recorded tumor characteristics, Eastern Cooperative Oncology Group performance status, the presence of multidisciplinary tumor board (MDTB) discussion, and the number of surveillance imaging studies in the 2 years before the HCC diagnosis as previously described.[18] From these data and the electronic Child-Turcotte-Pugh (eCTP),[21] Barcelona Clinic Liver Cancer (BCLC) stage[23] was calculated, and the presence or absence

of American Association for the Study of Liver Disease (AASLD)-compliant HCC surveillance[16] was determined.

HCC patients were matched (1:4) to contemporary non-HCC cirrhotic patients (receiving VA care in the same quarter as the HCC diagnosis) by using the %GMATCH SAS macro (Mayo Clinic, Rochester, MN) adapted as follows. Patient and controls were matched by CTP score (±1), human immunodeficiency virus status, Cirrhosis Comorbidity Score (±2), age (±10 years), Charlson-Deyo Comorbidity Index (CDI) (±1), gender, and the Veterans Aging Cohort Score (±5), with customized weights (4:4:2:1:1:1:1).[21,24–26] For 10 cases only 3 appropriately matched controls could be identified.

Cost Data

VA Health Economics Resource Center's (HERC) Average Cost Datasets were used to capture inpatient, outpatient, pharmacy, and non-VA Fee-Basis costs (paid by the VA) (Supplementary Methods).[27–30] We used visit Stop Codes (numeric categorization of clinic specialty) to assign costs for outpatient visits to specific specialties. For each case and its matched control, inpatient and outpatient costs were included in the analysis from the date of HCC diagnosis for up to 3 years after diagnosis, the date of death of the case, or December 31, 2012, whichever came first. In years subsequent to the death of the case, the costs for both the case and matched controls were designated as missing. Per-patient-per-year (PPPY) costs were calculated by dividing total costs for cases and controls generated during case follow-up time by the case follow-up time in years. All costs were adjusted to 2016 dollars.

Analysis

We estimated the main effect of case versus control on total cost of care cumulatively and in each of the 3 years after HCC diagnosis. Generalized linear models (GLMs) with a gamma distribution and log link function to restore log-normality were used in R[31] to evaluate cost models to assess for significant interactions between case versus control status and geographic region, eCTP class, MDTB, HCC surveillance, and BCLC stage. Models were tested for fit by bootstrapping using the boot-StepAIC package.[31,32] For multivariable GLMs to estimate total cost for cancer care, analyses were restricted to cancer cases. Incomplete 3-year cost data were present for 11% of cases diagnosed in 2010 who survived after December 31, 2012. Sensitivity analysis censoring these individuals showed no significant change in cost predictions (Supplementary Figure 1), and therefore uncensored data are presented.

Results

Patient Characteristics

Of 7011 ICD9-CM coded cases, 3988 cases were confirmed HCC and managed primarily within the VA system.[18] The 3183 HCC cases (79.8%) from an interim analysis were included in this cost analysis. Mean age of the predominantly male cohort was 61 years, with a demographic profile similar to the general VA population (Table 1). Cases were similar to controls with modest, expected differences with regard to underlying disease (higher hepatitis C virus infection in cases) and race/ethnicity (overrepresentation of blacks

among cases). BCLC 0/A/B/C/D stage was present in 6%/30%/41%/18%/16%, respectively. One-, 3-, and 5-year survival was 50.7%, 21.8%, and 11.2%, respectively.

Overall Cost

The mean 3-year total cost of care in HCC patients was $154,688 (standard error of the mean, $150,953–$158,422) compared with $69,010 (standard error of the mean, $67,344–$70,675) in age- and CTP-matched cirrhotic controls, yielding an incremental cost of $85,679 (Table 2); HCC 3-year costs exceeded 3-year costs incurred by an “average” veteran by $129,500.[33] Sixty-seven percent of the cost increment arose from inpatient costs, with a mean difference of $55,619 relative to controls. Incremental costs were modestly weighted toward the first year of care ($53,337). Overall, cancer-specific cost PPPY of life was $147,912. Costs for liver transplantation were dominant in the 92 transplanted cases (2.9%), with a 3-year incremental cost of $422,007 relative to controls and $396,735 over non-transplanted HCC cases (Table 2, Supplementary Table 1).

Effect of Cirrhosis Stage on Cost Estimates

Because progressive liver dysfunction impacts non-cancer-related healthcare costs in patients with advanced cirrhosis, we analyzed costs of HCC care stratified by CTP class. As shown in Figure 1*A*, although the total cost did not differ across CTP classes, the balance of inpatient to outpatient costs shifted markedly, with inpatient costs accounting for 60% of total costs in CTP A compared with 71% in CTP B and 83% in CTP C. CTP-matched controls showed a nearly identical distribution of inpatient and outpatient costs (A, 64%; B, 70%; C, 82%), and the case-control differences in cost showed a similar distribution. The average number of acute/subacute inpatient days in CTP A HCC cases was 53 (16 more than controls), compared with 67 in CTP B (34 more) and 72 in CTP C (44 more). Three subgroups of cost dominate the outpatient cost difference between HCC cases and controls (Figure 1*B*), those related to interventional radiology, pharmacy, and Fee-Basis Care. As expected, interventional radiology and Fee-Basis costs were less likely to be provided to patients with greater hepatic decompensation. The dominant source of increased pharmacy cost in all 3 subgroups was related to sorafenib: CTP A $7635 (70% of cost increase), CTP B $4304 (99%), and CTP C $2575 (39%). The difference in PPPY cost relative to controls was least in CTP A ($90,747 PPPY) compared with CTP B and C patients ($182,733 PPPY and $303,391 PPPY, respectively) (Supplementary Table 1, Figure 1*C*). These data suggest patients with advanced liver disease who develop HCC consume similar resources as compensated cirrhotic patients, but costs are concentrated in shorter time windows (displayed as PPPM costs in Supplementary Table 2) and largely incurred during hospitalization. Although a significant proportion of increased pharmacy costs, cancer-related pharmacy costs contribute only modestly to total outpatient costs, which are largely driven by interventional radiology-related charges.

Effect of Hepatocellular Carcinoma Stage on Hepatocellular Carcinoma-related Costs

We next explored the impact of cancer stage on cost. Similar total costs were found for early stages (BCLC 0–A) as well as in intermediate and terminal stages (BCLC B, D), with the lowest total cost for advanced stage (BCLC C) (Figure 2*A* and *C*, Supplementary Figure 1). Inpatient costs accounted for 61.9%–65.4% of costs for BCLC 0–C but 81.0% of BCLC D.

Outpatient costs were also similar for early stage disease (BCLC 0–A), with a mean of approximately $24,000 for interventional procedures and $16,000–$21,000 of pharmacy cost of which approximately $4000 arose from sorafenib (Figure 2*B*). For patients with BCLC B and C disease, interventional costs were significantly lower, as were overall pharmacy costs, with systemic therapy with sorafenib accounting for a larger fraction. Diagnosis at BCLC 0/A status was associated with markedly lower PPPY cost relative to more advanced stages because of longer survival times (Figure 2*C*); PPPY cost was $136,759, $132,764, $178,470, $269,312, and $466,758 in BCLC 0–D, respectively.

Other Drivers of Hepatocellular Carcinoma-related Costs

We next evaluated other variables that may be associated with differences in HCC-related costs. In univariable analyses, neither geographic region nor specific underlying liver disease (eg, alcohol or hepatitis C) was significantly associated with cost differences (data not shown). However, as shown in Table 3, individuals with combined alcohol/hepatitis C virus exhibited higher costs. Multidisciplinary tumor board management, receipt of AASLD-compliant liver cancer surveillance, and management at centers with academic affiliations were all associated with higher 3-year total costs and longer survival.

Development of Generalized Linear Model Cost Model

We next explored developed multivariable GLM models for predicting total HCC-related costs. Initial models included liver transplantation, CTP class, BCLC tumor stage, disease etiology, case discussion at a MDTB, cancer surveillance, and hospital academic affiliation including all potential interactions. In multivariable models, disease etiology, CTP class, and pre-diagnosis cancer surveillance were not independently predictive of total cost. Three highly predictive models including transplantation status, the interaction of BCLC status and MDTB, and the interaction of BCLC and academic hospital affiliation are presented (Supplementary Table 3), the simplest of which incorporates receipt of transplantation and BCLC cancer stage (Table 4). Predicted total costs, survival, and PPPY cost are presented in Table 4 and Supplementary Table 4. Transplantation was associated with greatest incremental cost, averaging an additional $365,645 over non-transplant care. Although MDTB was associated with a small but significant cost increase, significantly improved survival at each BCLC stage greater than BCLC ≥A resulted in significant reduction in the PPPY cost. Management of cases at a hospital with academic affiliation resulted in longer survival, associated with slightly lower costs in early stage disease, but higher costs in intermediate to late stage disease, and equivalent costs in BCLC D.

Discussion

We estimate that cost of care for HCC averages $154,688 during 3 years of follow-up, compared with $69,010 in age- and CTP-matched cirrhotic controls who do not develop cancer, yielding an incremental cost of $85,679. The estimated PPPY and per-patient-per-month cancer-specific costs were $147,912 and $12,326, respectively. Although it is difficult to compare VA with non-VA cost expenditures, most recent estimates are that VA costs are generally about 17% lower than costs incurred by Medicare.[34,35] Extrapolating to the U.S. population, the cancer-specific costs for treatment of 40,000 incident cases in 2016 would

have approximated $4.4 billion, and the total cost of care would have approximated $7.2 billion.

Our measurements of the costs related to HCC care significantly exceed most previous estimates. Some of the differences may reflect temporal evolution of treatments used for HCC, such as increased utilization of transarterial chemoembolization and sorafenib after 2008. The dominance of costs related to inpatient length of stay has never been previously observed, suggesting that comprehensive capture of these costs may also partially explain the higher costs. For instance, the most recent estimates from the SEER-Medicare registry in 2009 approximated $35,011 annual costs,[12] but the costs of cirrhosis and, in particular, inpatient care were extremely low, suggesting possible underestimation. Estimates of HCC annual costs from a managed care database yielded fairly similar results to the SEER-Medicare data, with $43,761 PPPY incremental cost over non-hepatitis C-infected individuals.[9] By contrast, our estimates are fairly similar to median costs derived from a smaller, single-center estimation of patients with HCC managed at a transplant center, in which median patient cost was $176,456.[7] In that series, non-transplant case median total cost was estimated at $91,505, and the incremental cost associated with transplantation was only ~ $100,000, both significantly lower than our estimates of $154,688 and $422,007, respectively, in a similar population. Possible reasons for the differential costs could include the nature of palliative/bridging interventions used, the comprehensiveness of cost accounting, or health system efficiencies.

Inpatient costs were notably dominant over outpatient costs, accounting for 65%–80% of HCC-related costs with an average of 26 additional hospital days for HCC patients over CTP-matched controls. The balance of treatment-related versus decompensation-related hospitalization days merits further investigation. Patients with more advanced CTP B–C cirrhosis incur higher inpatient costs, most likely related to management of hepatic decompensation events, and lower outpatient costs related to cancer treatment. Identifying patients at high risk for intervention-related decompensation that may be better managed with palliative care approaches could reduce morbidity, improve quality of life, and control costs.

Largely because of limitations of the SEER registry, few data explore the impact of clinically used liver cancer staging on outcomes and cost. Patients with early stage HCC (BCLC 0–A) accrued significantly higher costs than patients with intermediate to advanced stage disease, with lowest overall costs in BCLC C patients. Likely because BCLC includes CTP status, when both CTP class and BCLC stage were included in GLM cost models, CTP class yielded insignificant coefficients, thus allowing development of a simplified model that was based on transplantation and BCLC that accurately predicts 3-year costs. This model may be of use for health systems and third-party payers for predicting the impact of increased HCC incidence anticipated during the next decade on future liver disease-related costs.

Another novel finding was that care processes critically impact cost. Liver cancer surveillance, associated with more frequent detection of BCLC 0–A cases, was associated with increased costs. Increased costs with surveillance could reflect longer patient survival

or higher use of transplantation but also correlated significantly with management at academically affiliated centers and those with MDTB, factors that independently associated with cost. MDTB discussion correlated with higher costs but also with improvements in survival rates after adjusting for BCLC stage, resulting in lower PPPY costs ($174,484 versus $250,491). MDTB was most cost-efficient in non-transplanted BCLC C patients because of the strong impact of this process on survival (126-day increase). Unlike in the community, patient receipt of care at an academically affiliated VA is primarily determined by geography rather than socioeconomic status or motivation to seek tertiary care. We found that management at academically affiliated Vas had effects on cost independent of MDTB, with more efficient, lower cost care provided for early stage patients. By contrast, BCLC C patients managed at academic centers had significantly greater costs expended ($16,144), with a modest 41 days of survival gained. Only $6026 of this difference was directly attributable to sorafenib pharmacy costs. Therefore, we postulate that other interventions with high cost (eg, ^{90}Y-embolization, radiotherapy) but modest impact on survival potentially account for lower cost-efficiency in BCLC C.

Strengths of this study include cohort size, cohort characterization, comprehensiveness of cost acquisition, and completeness of capture of confounding variables. However, as with any observational cohort study, there is potential for unmeasured confounding. Veterans may have differential access to certain services as well as divergent survival outcomes than the general U.S. population. Although tumor staging was abstracted from chart review, ICD9-CM diagnosis codes and CPT codes were used to determine comorbidity, underlying liver disease, and treatments, possibly introducing misclassification bias. Cost accounting in the VA is not claims based and thus may be difficult to generalize because the costs of specific interventions (eg, a single episode of transarterial chemoembolization) are difficult to estimate.

Conclusion

HCC care consumes tremendous healthcare resources, likely higher than previously estimated. As HCC incidence increases and more expensive interventions are developed, the burden HCC places on U.S. healthcare will increase. The cost-effectiveness of therapies that can prevent HCC development by reducing progression to cirrhosis or by detecting cancer at earlier, curative stages should be re-evaluated in the context of these new comprehensive measurements of HCC-related costs.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations used in this paper

AASLD	American Association for the Study of Liver Diseases
BCLC	Barcelona Clinic Liver Cancer Stage
CDI	Charlson-Deyo Comorbidity Index
CPT	Common Procedural Terminology
eCTP	electronic Child-Turcotte-Pugh
GLM	generalized linear model
HCC	hepatocellular carcinoma
HERC	Health Economics Resource Center
ICD9-CM	International Classification of Disease-CM, version 9
MDTB	multidisciplinary tumor board
PPPY	per-patient-per-year
RBRVS	Resource Based Relative Value Scale
SEER	Surveillance Epidemiology and End Results
VA	Veterans Affairs

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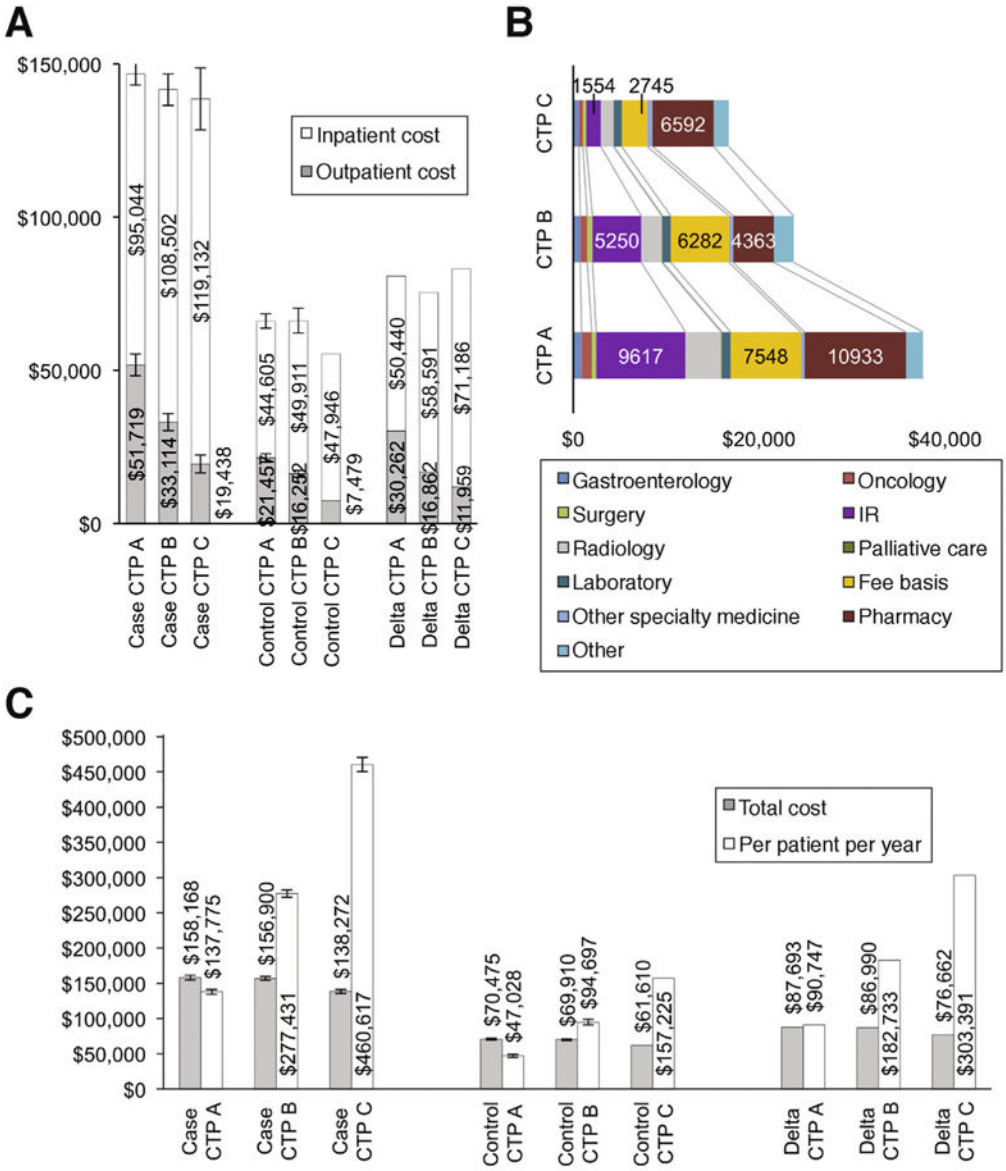

Figure 1.

HCC costs stratified by CTP status. (*A*) Three-year inpatient (*white bars*) and outpatient (*grey bars*) cost among CTP class A–C HCC cases, CTP-matched controls, and the case-control differences (Delta). (*B*) *Stacked columns* representing the difference in outpatient costs between cases and controls within cost subdomains with specific enumeration of costs from interventional radiology (*IR*), Fee-Basis, and pharmacy costs. (*C*) Three-year cost and PPPY cost among CTP class A–C HCC cases, CTP-matched controls, and the case-control differences (Delta). All *error bars* reflect standard error of the mean.

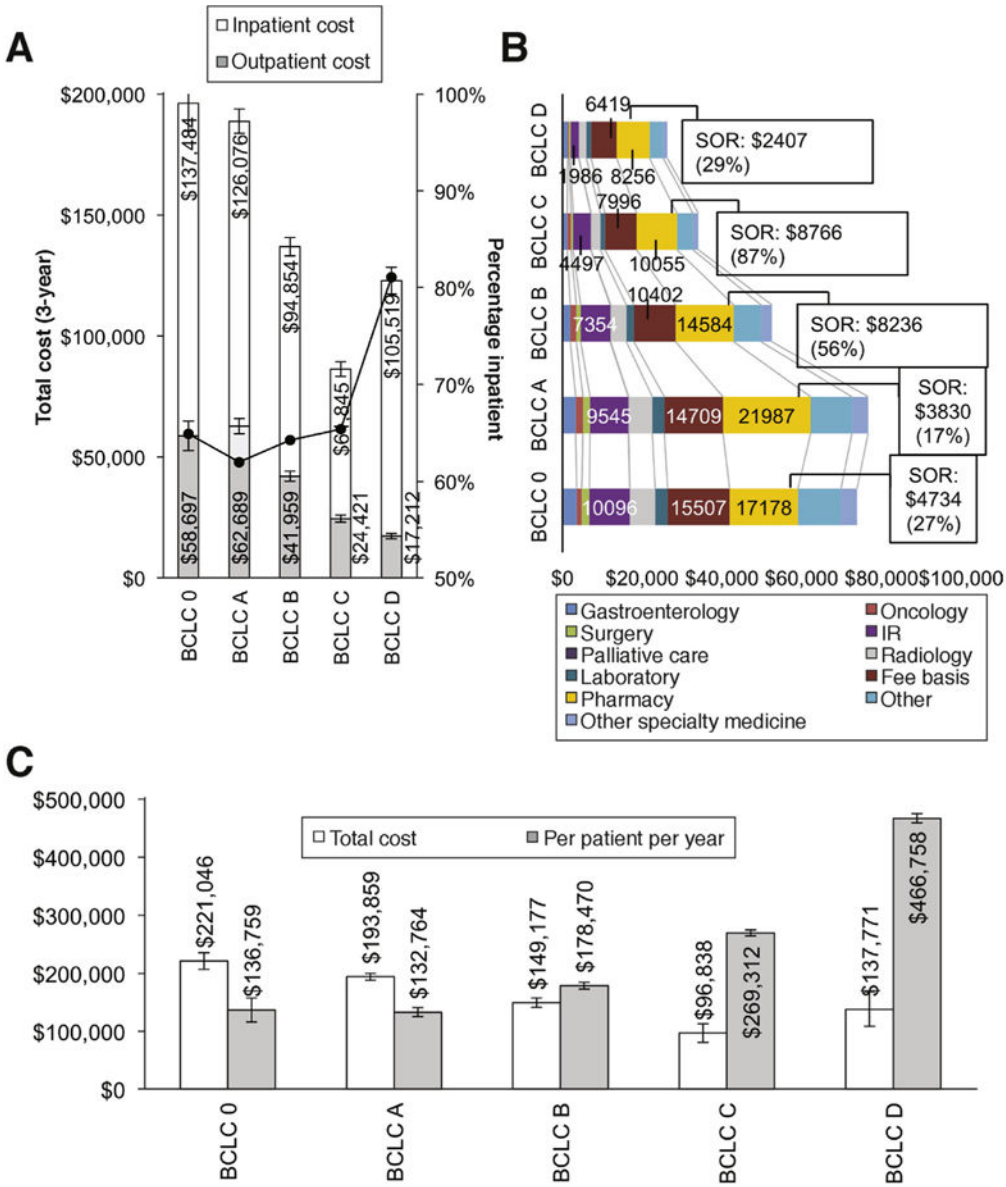

Figure 2.

HCC costs stratified by BCLC cancer stage. (*A*) Three-year inpatient (*white bars*) and outpatient (*grey bars*) cost across BCLC stages. *Line* represents percentage of costs related to inpatient care. (*B*) *Stacked columns* representing outpatient costs across BCLC stages within cost subdomains with specific enumeration of costs from interventional radiology (*IR*), Fee-Basis, and pharmacy costs. The fraction of pharmacy costs related to sorafenib (*SOR*) is provided. (*C*) Three-year cost and PPPY cost across BCLC Stages are presented. All *error bars* reflect standard error of the mean.

Table 1

Baseline Patient Characteristics

Variable	Case	Controls
N	3183	12,722
Age, *y* (mean SD)	61.3±7.7	60.9±7.4
Age difference from cases (mean ± SD)		−0.4 ± 1.9
Gender (M/F)	3169/14	12,704/56
Underlying liver disease		
Hepatitis C only (N, %)	860 (27)	2893 (23)
Alcohol only (N, %)	345 (11)	3196 (25)
Hepatitis C and alcohol (N, %)	1601 (50)	4982 (39)
Hepatitis B (N, %)	38 (1)	96 (1)
Nonalcoholic steatohepatitis (N, %)	68 (2)	N/A[a]
Other or unknown (N, %)	262 (8)	1593 (12)
Ethnicity		
White (N, %)	1808 (57)	8547 (67)
Black (N, %)	755 (24)	2016 (16)
Asian (N, %)	12 (<1)	31 (<1)
Hispanic or Hispanic black (N, %)	264 (8)	1066 (8)
Other or unknown (N, %)	351 (11)	1100 (9)
eCTP		
A (N, %)	1703 (54)	6816 (53)
B (N, %)	1129 (35)	4528 (35)
C (N, %)	351 (11)	1416 (11)
CTP score difference from cases (mean ± SD)		0.004 ± 0.290
Comorbidity		
CDI (mean ± SD)	1.6 ± 1.6	1.3 ± 1.5
CDI difference from cases (mean ± SD)		−0.3 ± 1.2
Cirrhosis Comorbidity Index (median)	1 + 0	1 + 0
CirCom class difference from Cases (Mean ± SD)		−0.03 ± 0.59
Tumor characteristics		
No. (mean ± SD)	2.4 ± 1.7	
Largest tumor size, *cm* (mean ± SD)	4.8 ± 3.5	
Macrovascular invasion (N, %)	605 (19)	
Extrahepatic spread (N, %)	223 (7)	
BCLC		
0 (N, %)	180 (6)	
A (N, %)	948 (30)	
B (N, %)	990 (31)	
C (N, %)	568 (18)	
D (N, %)	497 (16)	
Surveillance		N/A[a]

Variable	Case	Controls
AASLD-adherent	802 (26)	
Sporadic or none	2309 (74)	
Case presented at MDTB		
No	2062 (66)	
Yes	1121 (36)	
Case managed at center with academic affiliation		
No	980 (31)	4725 (37)
Yes	2203 (69)	7921 (63)

SD, standard deviation.

[a]Data obtained through manual extraction, only available for HCC cases.

Table 2

Overall Costs and Costs Stratified by Receipt of Liver Transplantation

	Case	Control	Difference	*P* value
All				
N	3183	12,722		
3-year total cost, mean, *$* (95% CI)	154,688 (150,953–158,422)	69,010 (67,344–70,675)	85,679	<.0001
Outpatient, *$* (total)	41,560 (39,671–43,448)	18,069 (17,248–18,890)	23,491	<.0001
Pharmacy, *$*	14,204 (12,472–15,935)	6080 (5339–6821)	8124	<.0001
Interventional radiology, *$*	7402 (6669–8133)	223 (201–245)	7179	<.0001
Radiology, *$*	4140 (4066–4214)	1155 (1134–1176)	2986	<.0001
Other outpatient, *$*	7072 (6898–7245)	5154 (5027–5280)	1918	<.0001
Laboratory, *$*	2068 (2028–2108)	1171 (1150–1194)	896	<.0001
Oncology, *$*	1248 (1115–1379)	356 (319–394)	891	<.0001
Gastroenterology/hepatology, *$*	2233 (2174–2292)	1401 (1365–1439)	832	<.0001
Palliative care/hospice, *$*	103 (95–113)	6 (6–7)	97	<.0001
Surgery, *$*	1226 (1145–1305)	740 (691–788)	486	<.0001
Specialty medicine, *$*	2708 (2624–2791)	2278 (2208–2349)	429	<.0001
Inpatient, *$*	102,474 (99,568–105,381)	46,856 (45,526–48,184)	55,619	<.0001
Inpatient days	60 (57–63)	34 (33–36)	26	<.0001
% Fee-Basis	6.9 (6.6–7.2)	5.9 (5.7–6.2)	1.0	<.0001
Year 1 cost, mean, *$* (95% CI)	$98,240 ($96,254–$100,227)	44,904 (43,996–45,812)	53,337	<.0001
Year 2 cost, mean, *$* (95% CI)	37,945 (35,776–40,114)	17,054 (16,079–18,029)	20,891	<.0001
Year 3 cost, mean, *$* (95% CI)	18,504 (17,478–19,529)	7053 (6662–7444)	11,450	<.0001
Median survival (*days*)	493.9			
PPPY, mean, *$* (95% CI)	223,723 (217,876–229,570)	75,811 (73,829–77,792)	153,547	<.0001
Non-transplant				
N	3091	12,354		
3-year total cost, mean, *$* (95% CI)	143,220 (139,804–146,638)	67,553 (65,942–69,164)	75,667	<.0001
Median survival (*days*)	480			
PPPY, mean, *$* (95% CI)	222,878 (216,995–228,760)	76,668 (74,645–78,692)	146,209	<.0001
Transplant				
N	92	368		
3-year total cost, mean, *$* (95% CI)	539,955 (465,300–614,610)	117,948 (101,641–134,256)	422,007	<.0001
Median survival (*days*)	966			
PPPY, mean, *$* (95% CI)	252,122 (213,551–290,694)	47,002 (39,811–54,193)	205,120	<.0001

Table 3

Impact of Disease Etiology, Tumor Board Discussion, and AASLD-compliant Surveillance on 3-Year Total Costs

Variable	N	Total cost, *$* (SE)	Mean survival (*days*)	PPPY, *$* (± SE)	GLM *P* value (total cost)	GLM *P* value (PPPY)
Etiology of liver disease						
EtOH	322	116,562 (107,958–125,166)	415.6	242,033 (222,255–261,811)		
EtOH + HCV	1599	175,971 (170,142–181,800)	539.3	224,464 (216,233–232,695)	<.0001	.43
HCV	856	145,260 (138,684–151,837)	542.6	204,736 (194,475–214,998)	.86	.80
HBV	60	120,364 (99,782–140,946)	512.2	229,447 (186,011–272,883)	.01	.09
Other	346	127,896 (118,789–137,003)	437.3	249,237 (229,589–268,885)	.36	.80
MDTB[a]						
No	1121	141,899 (137,663–146,135)	471.9	250,491 (242,581–258,402)		
Yes	2062	180,313 (173,012–187,613)	597.4	174,484 (167,010–181,957)	<.0001	<.0001
AASLD-compliant liver cancer surveillance[a]						
No	2309	145,871 (142,004–149,739)	485.8	238,887 (231,666–246,109)		
Yes	874	183,799 (175,402–192,197)	605.9	178,702 (169,394–188,010)	<.0001	<.0001
Academic affiliation						
No	980	143,696 (137,486–149,905)	416.7	258,681 (246,494–270,867)		
Yes	2203	160,647 (156,017–165,277)	528.2	208,172 (201,631–214,713)	<.0001	.003

EtOH, alcoholic liver disease; HBV, chronic hepatitis B; HCV, chronic hepatitis C; SE, standard error.

[a]Obtained from manual chart extraction.

Table 4

GLM Model, Predicted Total Costs, Survival, and PPPY Costs

	Variable	Estimate	Standard error	*P* value	Function and performance	
Model	(Intercept)	12.0674	0.0860	<.0001	GLM formula = fitVAR ~ Transplant + BCLC,	
	Transplant = Y	1.2192	0.1230	<.0001	family = Gamma (link = log)	
	BCLC A	−0.0057	0.0934	.95		
	BCLC B	−0.1665	0.0934	.075	AIC 82027 null deviance 3345.2 on 3182 degrees	
	BCLC C	−0.5950	0.0986	<.0001	of freedom; residual deviance: 2956.5 on 3172 df	
	BCLC D	−0.3424	0.1000	.0006		
Prediction	BCLC	Transplant	N	Total cost, *$* (SE) (3-year) Mean	survival, *days* (±SE)	PPPY (±SE)
	0	N	169	174,107 (159,134–189,079)	738 (691–784)	130,240 (116,132 −144,347)
	A	N	892	173,120 (166,536–179,703)	698 (679–718)	130,307 (124,065–136,549)
	B	N	985	147,404 (142,019–152,789)	485 (472–498)	178,004 (169,813–186,196)
	C	N	566	96,034 (91,403–100,665)	257 (248–266)	267,139 (250,911–283,367)
	D	N	479	123,621 (117,224–130,018)	212 (204–220)	458,435 (428,554–488,317)
	0	Y	11	589,236 (504,518–673,953)	1503 (1345–1661)	195,726 (160,279–231,173)
	A	Y	56	585,896 (514,657–657,135)	1422 (1296–1549)	195,827 (165,834–225,819)
	B	Y	5	498,864 (435,160–562,568)	989 (897–1082)	267,507 (224,478–310,536)
	C	Y	2	325,012 (282,208–367,815)	524 (474–575)	401,460 (334,862–468,058)
	D	Y	18	418,375 (364,298–472,452)	432 (391–473)	688,943 (576,773–801,112)

N, no; Y, yes.