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The Cost of Palliative Care for Hepatocellular Carcinoma in Hong Kong

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Abstract

Background: Hepatocellular carcinoma (HCC)is endemic in parts of Asia and Africa and most patients are not suitable for treatment with a curative approach. Little is known about the cost of palliative care for HCC.

Objective: To determine: (i) patient-specific costs of palliative care of HCC; and (ii) individual factors that drive patient-specific costs and to develop a model of cost per case under alternative circumstances.

Methods: 204 patients with inoperable HCC were prospectively tracked from first hospitalisation until death for health service utilisation. A societal perspective of cost was taken, including costs of formal and informal services incurred by payers, caregivers and patients. Observational data from a large Hong Kong cancer care programme were used. A regression analysis was performed using formal costs only, with the cost per observed day as the dependent variable.

Results: The median survival was 95 days and the mean observation period was 153 days. The mean value per person for formal healthcare cost was 30 983 Hong Kong dollars [$HK] ($US3872, 1998 values). The distribution of cost values were positively skewed. The regression analysis showed that age, days of observation and survival were negatively related to cost per observed day, and the Child-Pugh grading of severity of liver cirrhosis was positively related to cost per observed day. A sensitivity analysis based on the regression equation indicated that non-survivorship doubles the cost per case, increased severity as measured by the Child-Pugh Index adds about 50% to the cost, and chemotherapy increases cost 2-fold.

Conclusions: The relatively modest average cost per patient with HCC in Hong Kong reflects the short median survival and subsequently the limited use of in-patient care and chemotherapy.

Hepatocellular carcinoma (HCC) is one of the world's most common cancers with a particularly high incidence in parts of Africa and Asia.[1] In Hong Kong, it is the second most common malignancy with an age-standardised incidence rate of 24.1 per 100 000 individuals.[2] With a population of 6 000 000 in Hong Kong, 1707 new case reports of HCC were registered in 1994.[2]

Surgical resection is the only potentially curative form of therapy; however, only 10% of patients have an operable stage of disease at presentation.[3] Of the remainder, a further 30% (based on experience at Prince of Wales Hospital) can be offered active noncurative (i.e. palliative) treatment that comprises locoregional therapies such as chemoembolisation or selective internal irradiation, and intravenous systemic chemotherapy.[4] Patients with HCC who have the poorest liver function on presentation (around 60%) are not candidates for active treatment and therefore receive best supportive care. During the course of best supportive care, the patients may be transferred to an extended care facility or a hospice care facility.

Very little is known about the cost of care for HCC. Four groups of investigators[5-8] conducted studies that were based on the assignment of costs to specific care protocols, and thus were not based on observation. Two observational studies examined the hospital costs of end-stage liver disease (but not HCC)[9] and the social costs of colorectal cancer with liver metastases.[10] Neither addressed the specific treatment issues of HCC.

The present study had 2 objectives. The first was to determine the patient-specific costs of palliative care of HCC from a societal perspective using observational data from a large Hong Kong cancer care programme. The second was to determine the individual factors that drive patient–specific costs, including patient age, severity of liver cirrhosis and treatment modality, and to develop a model of cost per case under alternative circumstances, including varying lengths of survival, survival or nonsurvival, and mode of care.

Methods

Patients and Follow-up

This study included all patients with HCC who presented to the Department of Clinical Oncology, Prince of Wales Hospital, a 1337-bed teaching hospital in Hong Kong, between June 1996 and May 1997. The Prince of Wales Hospital is a publicly funded hospital, and all cancer-related services are provided free of charge. Excluded were about 10% of patients who were treated surgically with curative intent during this period and who did not reenter the study. The diagnosis of HCC was made either by histological examination of tumour tissue, or imaging evidence of a space-occupying lesion in the liver together with a serum α-fetoprotein level of above 500 g/L in a known carrier of the hepatitis B virus surface antigen. Patients were enrolled during their first admission to hospital and were thereafter tracked until death or loss to follow-up.

The severity of cirrhosis was classified at the time of first hospital admission according to Child-Pugh grading (table I). The choice of subsequent palliative strategy was determined at a Joint Hepatoma Clinic (including radiologists, oncologists and surgeons) after discussion with the patients. The strategies included best supportive care or active noncurative strategies for patients with Child-Pugh grades A and B cirrhosis. For patients with Child-Pugh grade C cirrhosis, best supportive care was considered the only appropriate strategy.

All the data for health service utilisation was

Table I. Severity of liver disease (Child-Pugh's grading)[11][a]

Clinical and biochemical measurements	Points scored for increasing abnormalities		
	1	2	3
Encephalopathy	None	1 and 2	3 and 4
Ascites	Absent	Slight	Moderate
Bilirubin (mg/100ml)	1–2	2-3	>3
Albumin (g/L)	>35	28-35	<28
Prothrombin (seconds prolonged)	1-4	4-6	>6

a Graded according to total points score. A: score 5 to 6; B: 7 to 9; C: 10 to 15.

collected prospectively by the research nurses. From the date of accrual, all patients were interviewed once per month until death or until the last follow-up.

Analytical Approach

A societal perspective was taken that included all formal and informal services incurred by payers, caregivers and patients. The cost of any specific services that were used by a patient had 2 components: the number of units of services that were used by the patient, and the cost of each of these units. Measured resources included short-term inpatient hospital care, continuing inpatient care and hospice care, outpatient services (clinics, diagnostic tests, and drugs), Chinese and herbal medicines, supplies privately obtained, and the income lost by caregivers and patients. All costs are expressed in terms of Hong Kong dollars ($HK1 = $US0.125; 1998 values).

All hospital and extended inpatient care was measured in terms of patient days. Costs for the number of short term inpatient days were valued in terms of the per diem total cost for a cancer ward (including physician services, diagnostic services, pharmaceuticals and an overhead allocation) according to the methodology developed by the Hospital Authority of Hong Kong. Costs for extended care hospital days (including palliative care) were valued according to the average inpatient cost per day (including an overhead allocation) for each facility.

Outpatient care was divided into three categories – clinic visits (routine visits, chemotherapy visits, and chemotherapy follow-up visits), pharmaceuticals, and diagnostic services. Outpatient clinic costs included nursing and physician costs and supplies, and were derived as a cost per visit, averaged over a sample of clinic days. The cost of outpatient drugs was based on the formulary cost at the Prince of Wales Hospital, and included an additional cost per prescription for professional pharmacists' services. Diagnostic services were valued in terms of workload units. Laboratory workload units for each type of test were based on the WELCAN[12] workload system. The cost per workload unit was based on the cost for the Prince of Wales Hospital laboratory. Radiological services were based on the diagnostic imaging common procedure/examination list of Alberta Health, Canada.[13] Per minute technical costs were estimated by the Prince of Wales Hospital radiology services unit.

Informal services and indirect costs were measured using personal interviews. Respondents were directly contacted and were requested to estimate informal healthcare resources, including the amount spent for Chinese and herbal medicines, supplies related to their illness, and the loss of income from work for both patients and for caregivers. The respondents were interviewed once per month by one of the study nurses.

For our descriptive analysis, we calculated the mean value and distribution of costs, by service or type of resource, for those who used each type of service or resource. A predictive (regression) analysis was conducted only for formal healthcare services because of the lack of additional variables which could be used to predict personal out-of-pocket and indirect costs. As some patients were lost to follow-up, we used a cost per day of observation (total formal cost divided by days of observation) as our dependent variable. Independent variables included patient age, Child-Pugh grading at hospitalisation (Child-Pugh grades A and B versus grade C), period of observation (admission to hospital until death, loss of follow-up, or conclusion of observation period), type of intervention (chemotherapy and locoregional therapy versus best supportive care) and nonsurvival versus survival at the end of the observation period or loss to follow-up. As we found that this dependent variable had a nonlinear relationship with our predictors, all regression solutions used natural log transformations of costs. Based on the regression results, we developed a sensitivity analysis for measures of cost per case using a number of alternative scenarios.

Results

Descriptive Analysis

204 patients were recruited and their characteristics are listed in table II. The mean age was 57 years (139 were under 65 years of age) and 169 were male; 129 patients were classified as Child-Pugh grades A or B, and 75 patients were classified as grade C. A total of 135 patients died within the observation period; 14 survived beyond the observation period, and 55 were tracked until the last follow-up visit or before being lost to our follow-up attempts. Of those lost to follow-up, 13 died in Hong Kong outside of study sites, 18 died in mainland China, and contact was lost with 24. The median survival was 95 days. The mean observation period was 153 days [standard deviation (SD) 171 days]. Given that the duration of observation distribution was skewed to the right, the median was much less than the mean – 65 days. A total of 136 patients received best supportive care and 68 received active noncurative treatment as the first treatment following enrolment. Of the 68 who received active noncurative treatment, 37 received intravenous systemic chemotherapy and 31 received locoregional treatments.

Table II. Patient demographic and disease characteristics of the study sample

Characteristic	Value	% of group
Number of patients	204	
Age		
Mean (y)	57.15	
Standard value (y)	13.38	
Number <65y	139	68
Number ≥65y	65	32
Sex		
Male	169	83
Female	35	17
Child-Pugh Grade		
Grade A and B	129	63
Grade C	75	37
Outcome		
Death	135	66
Continuing	14	7
Lost to follow-up	55	27
Observation period (days)		
Mean	153	
Standard deviation	171	
Median	65	
Minimum	1	
Maximum	733	
Initial treatment at enrolment into study		
Best supportive care (palliative)	136	66.6
Noncurative treatment		
locoregional therapies	37	18.1
systemic therapies	31	15.2

The types of healthcare services provided to the 204 patients were as follows: a total of 114 patients were treated in both hospital inpatient and outpatient settings; 45 patients were treated in 3 settings – inpatient care, outpatient clinic, and nursing homes; 23 in hospital only, without any other services; 17 in inpatient hospital and nursing home only, and 5 in all 4 settings – inpatient and outpatient (clinic) hospitals, nursing homes and home care.

Patient costs by type of service are summarised in table III. The mean value for formal inpatient short term stay care costs was $HK19 581 ($US2481). This value also was markedly skewed with a median value of $HK11 680 ($US1460). The mean number of inpatient days per patient was 8.5 (SD 9.8). The average stay for inpatient nursing care was 16.4 days and for inpatient hospice care it was 6.5 days.

A total of 177 persons received some component of outpatient services. Over all patients, including those who did not receive any outpatient services, the mean patient cost was $HK3158 ($US394; 1998 values), excluding chemotherapy. The distribution for outpatient costs was skewed to the right. For those who received some outpatient services, the mean values for each type of service are shown in table III. Patients who made outpatient visits averaged 11.5 visits.

With regard to informal costs, 93 persons incurred transport costs, at a mean value of $HK1168 ($US146). 10 patients incurred costs for Chinese herbal medicines (mean value of $HK10 795 or

Table III. Patient costs ($HK; 1998 values)

Cost component	Number of cases (with costs > 0)	Mean cost (for those with costs > 0)	Standard deviation	Mean cost over all cases (% of total)
Formal costs				
Inpatient – acute care	204	19 581	23 049	19 851 (33.6)
Continuing inpatient care	68	20 782	22 489	6927 (11.7)
Outpatient care				
accident and emergency	81	1105	1427	439 (0.1)
outpatient clinic – cancer clinic	116	1937	2692	1101 (1.8)
outpatient clinic – diagnostic	136	1051	1851	701 (1.1)
outpatient clinic – drugs	124	1509	1916	917 (1.5)
chemotherapy	31	8661	4933	1316 (2.2)
Total formal costs				31 252 (52.9)
Informal costs				
Patient loss of income	62	83 734	96 970	25 449 (43)
Caregiver loss of income	11	8500	8574	458 (0.8)
Transportation	93	1168	3575	532 (0.9)
Herbal/Chinese medicine	10	10 795	11 689	529 (0.9)
Private costs	28	6210	10 191	852 (1.4)
Total informal costs				27 821 (47.0)
Total costs (formal + informal)				**59 073 (100)**

HK = Hong Kong.

$US1349) and 28 incurred other healthcare costs (mean value of $HK6210 or $US776). With regard to indirect costs, 62 patients reported a loss of income, with a mean value of $HK83 734 ($US10 466) during the observation period. There was a wide variation with 12 patients having costs under $HK30 000 ($US3750) and 6 over $HK200 000 ($US25 000). 11 caregivers incurred indirect costs of $HK8500 ($US1062) per caregiver. The costs were nearly split evenly, with formal costs accounting for 52.9% and informal costs 47.1% of the total.

The mean value per person for healthcare system costs was $HK30 983 ($US3872). The standard deviation was $HK30 768 ($US3846). The mean value of the cost per observed day was $HK1049 ($US131) with a standard deviation of $HK1702 ($US212).

Regression Analysis

The regression analysis was conducted using healthcare system costs only. The results of the regression analysis are shown in table IV with predicted costs specified in log form. The number of days of observation, age, and survival were negatively related to unit cost, while the Child-Pugh grading and the two active treatment therapies (systemic or logoregional) were positively related. All variables were significant at the 0.05 level or better.

The relationship between cost per day (transformed from logarithmic into actual values) and the number of observed days was estimated from the regression equation for a base case (see table V for base case assumptions). The estimated cost per case for the base case was $HK40 052 ($US5006). A one-way sensitivity analysis, which was conducted by changing individual assumptions, indicated that cost per case was quite sensitive to survival, severity, chemotherapy and locoregional therapy. The highest projected cost per case was $HK85 800 for the base case with chemotherapy, and the lowest was $HK 19 379 for the base case (except the patient survived). Thus, nonsurvivorship doubles the cost per case, increased severity as measured by the Child-Pugh Index (grade C) adds about 50% to the cost, and chemotherapy increases the costs two-fold (table V).

Table IV. Regression analysis results. Dependent variable: log of cost per observed day ($HK; 1998 values)

Variable	Coefficient	Standard error[a]
Constant	10.79	0.87
Child-Pugh grade (A or B = 0, C = 1)	0.43	0.14
Observed days	–0.70	0.04
Age	–0.54	0.21
Systemic chemotherapy (no = 0, yes = 1)	0.76	0.17
Locoregional therapy (no = 0, yes = 1)	0.49	0.17
Survival or lost to follow-up (yes = 0, no = 1)	–0.72	0.12
R^2	0.77	

a Indicates coefficient is significant at α level of 0.05.

Discussion

In this study we developed an observational data base for the palliative care of patients with HCC who presented to a large public Hong Kong hospital. We included costs of healthcare services and other, related costs (including transportation, herbal and Chinese medicines and indirect costs of time loss for patients and caregivers). Our results showed that healthcare system costs average $HK30 983 ($US3872). We also developed a predictive model of formal costs. In this model, age, the severity of cirrhosis on presentation, the observational period, and the treatment modality were all significantly related to the cost per day.

Most patients with inoperable HCC have a background history of liver cirrhosis, and advanced HCC exacerbates the severity of cirrhosis resulting in a variety of complications in the terminal stages of the disease. It is therefore not surprising that the cost of palliative care for patients with HCC presenting with Child-Pugh grade C is higher than the cost of palliative care for patients with HCC presenting with Child-Pugh grades A and B.

Patients with Child-Pugh grades A and B who receive active noncurative treatment strategies incur only moderately greater costs per day than patients with Child-Pugh grades A and B who are given best supportive care. None of the active noncurative strategies have been shown to prolong survival in a randomised setting;[14-16] even a modest improvement in disease-free survival for those on active therapy might warrant the additional costs.

Nonsurvival was shown to be correlated with costs. This finding is consistent with the presence of an expenditure 'bubble' just prior to death, which has been noted by some investigators.[17] The costs for those who are lost to follow-up would therefore understate the cost of the disease, since these observations do not include the expenditure bubble.

Three previous studies presented estimates for the cost of HCC, although none were based on direct observation. Where possible, we have tried to standardise the results of these studies to those which we developed, by adjusting for survival or

Table V. Sensitivity analysis

Specifications of scenario	Projected cost per case	
	$HK (1998 values)	$US (1998 values)
Base case: 150-day survival period, age 59y, Child-Pugh Index A or B, non-survivor and not lost to follow-up, no chemotherapy, locoregional therapy	40 052	5006
Base case, except the patient survived	19 379	2422
Base case except 50-day survival period	28 869	3609
Base case except 100-day survival period	35 400	4425
Base case except 200-day survival period	43 600	5450
Base case except 250-day survival period	46 500	5813
Base case except Child-Pugh Index = C	61 650	7706
Base case with chemotherapy	85 800	10 725
Base case, but without locoregional therapy	24 300	3038

$HK = Hong Kong dollars.

observation time. The 6-month estimate of treatment costs by Sarasin et al.,[8] for Swiss patients, was $US36 000 (1994 values); this estimate included a hospital stay for palliative care of $US35 000. Kim et al.[5] derived their estimates from US national data; they estimated costs for HCC to be $US10 000 per annum (1994 values). Shiell et al.[7] estimated the cost of a treatment protocol to be Australian $A117 000 ($US61 000) [year of costing not stated]. The time period was not specified for this protocol. We also note 2 observational studies on liver-related disease: a US analysis by Wong et al.[9] on the hospital costs of end-stage liver disease (primarily oesophageal varices) and a well-conducted UK study on the societal costs of liver metastases in colorectal cancer.[10] In the latter study survival-adjusted costs were similar to those of our study, though treatment processes do differ.

The major omissions of our analysis were those of the diagnostic phase of the treatment, the cost of investigational agents, and missing follow-up data. The inclusion of diagnostic costs would not impact on early interventions, since similar costs would be incurred, only earlier. These costs would be relevant, in a decision-making phase, to cancer prevention. The costs after loss to follow-up would likely be higher than prior to follow-up, as the expenditure bubble would occur at that time. We have adjusted for this by including survival in the regression analysis.

Conclusion

The relatively modest average cost per patient with HCC in Hong Kong reflects the very short median survival and, subsequently, the limited use of inpatient care and chemotherapy in these patients relative to those with other diseases treated for extended periods.

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