Original Article

Curative and Survival Rates of Hepatocellular Carcinoma in Rajavithi Hospital between 2013 and 2017

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Background: Hepatocellular carcinoma (HCC) is a common cause of death in Thailand, and its high incidence rate is related to chronic hepatitis B virus (HBV) infection. Overall, the worldwide survival rate is increasing, but in Thailand, outcomes remain poor.

Objective: Rajavithi Hospital is a referral center, and this descriptive study reviewed the background data of patients who were referred here between 2013 and 2017. The objective of this study was to evaluate resectable rates and survival after hepatic resection.

Materials and Methods: The records were retrospectively reviewed of all 531 HCC patients treated in Rajavithi Hospital during the period January 2013 to June 2017. Clinical information, biochemical tests and radiologic findings were recorded, and descriptive data were presented as percent, mean, median and standard deviation (SD). Survival rates were estimated by the Kaplan-Meier method.

Results: 138 HCC patients had successful hepatic resection. We classified patients in accordance with Barcelona Clinic Liver Staging (BCLC), and we found that 1.4%, 29.0%, 38.4% and 31.2% were in stages 0, A, B, and C respectively. The overall survival rates after 1, 3, and 5 years of HCC patients who underwent resection were 74.0%, 60.0% and 59.4% respectively.

Conclusion: Chronic HBV infection is a significant risk factor of HCC in Thai patients, most of whom present at a late stage, resulting in inferior long-term outcomes. Prevention of HBV transmission and enhanced effectiveness of screening programs for high-risk patients could be important ways to reduce the mortality rate among Thai patients.

Keywords: Hepatocellular carcinoma, Hepatectomy

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Liver tumors are the fifth most common cause of death. Nowadays, there are many varieties of treatment for HCC depending on tumor characteristics and underlying liver disease; nevertheless, liver resection is still the therapeutic gold standard used to increase patient survival rates. Before 2000, the resectability rate for HCC in Thailand[(1)] was a mere 15.8% with median survival of 20.4 months. During the last few decades, the development of precise preoperative evaluation and new surgical techniques and instruments are among several factors which have contributed to reducing mortality after hepatectomy to less than 5% worldwide[(2,3)]. Rajavithi Hospital is a tertiary care center to which patients are referred for treatment, but at the time of writing, there has been no sizeable data-oriented study of HCC treatment in the hospital. This study provides data-oriented information for future research.

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The primary objective of this study was to evaluate the resectability rate of HCC patients in Rajavithi Hospital between 2013 and 2017, and the secondary aim was to evaluate survival rates after hepatectomy.

Materials and Methods

Data source

A retrospective descriptive study was performed, reviewing the Rajavithi Hospital database for operative data during the period January 2013 to June 2017.

Patient selection

Inclusion criteria were HCC patients who were first diagnosed in Rajavithi Hospital or were referred here for initial treatment including surgery and non-surgery treatment between 1 January 2013 and 30 June 2017. The exclusion criteria were recurrent tumor, or pathological report showing negative for HCC.

Data analysis

Data regarding age, gender, etiology, underlying liver cirrhosis or other disease, laboratory data, investigation data, choice of treatment, complications and pathologic report were

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garnered from a review of patients' medical records. Data were examined to establish operative time and estimated blood loss, and the District Office was contacted to determine dates and causes of death. Statistical analyses were performed using IBM SPSS version 22.0. Descriptive data were presented as percent, mean, median and SD, and survival rates were estimated by the Kaplan-Meier method.

Ethics statement

The study was reviewed and approved by the institutional review board of Rajavithi Hospital. The treatment planning was performed by a multidisciplinary team, and all patients underwent standard pre-operative examination and preparation. Informed consent was obtained before surgery.

Diagnostic criteria

Diagnosis was based on the American Association for the Study of Liver Disease (AASLD) 2018 guidelines[4]. Diagnosis of cirrhosis was performed by examining typical patterns on imaging CT or MRI. In dubious cases, we used liver biopsy before performing the operation.

The technique of liver resection used included both open hepatectomy and its laparoscopic counterpart.

Results

Clinical and laboratory profiles

The study included a total of 531 HCC patients with mean age of 57.54±11.43 years old. There were more than twice as many males as females (77.4% vs. 22.6%), and HBV-related HCC was the most common underlying liver disease at 51.4%, followed by HCV-related HCC at about 26.4%. Patients who had combined hepatitis B and hepatitis C infection accounted for 4.5% of subjects, while other causes such as alcohol or NASH represented 17.7% (Table 1). The most common presentation was abdominal pain at 62.7%, and we found that 27.3% of patients who underwent a screening program for HBV and HCV infection were asymptomatic (Figure 1). The majority of HCC patients were diagnosed by typical CT characteristics (91.4%), MRI (14.4%), and biopsy (5.2%). Patients with a single tumor accounted for 64% of cases, and these mostly dominated in the Rt lobe. Multifocal disease (>4 tumors) was found in 16.2% of patients. The use of surgical treatment for HCC patients is showing an upward trend: resectability rates were 19.8%, 13.8%, 40.4%, 46.6%, and 46.3% in 2013, 2014, 2015, 2016 and 2017 respectively (Figure 2).

One hundred and thirty-eight HCC patients underwent successful hepatic resection. We classified patients in accordance with Barcelona Clinic Liver Staging (BCLC), and we found that 1.4%, 29.0%, 38.4% and 31.2% were in stages 0, A, B, and C respectively. As shown in Figure 3, the most common operation was right hepatectomy (41%), and 17.3% of hepatic resection cases were performed with a laparoscopic technique. The conversion rate in laparoscopic hepatectomy was 25% (n = 8). The mean operative time in open surgery was 3.8 hours compared with 4.1 hours in laparoscopic procedures. The mean estimated blood loss was 850 cc, and the overall 90-day mortality rate was 3.6% (Table 3). In cases of non-surgical treatment, most patients (55.4%) received transarterial chemoembolization (TACE) or radiofrequency abrasion (RFA) (7%), while 10.3% of

Table 1. Demographic data of HCC patients in Rajavithi Hospital 2013 to 2017 (n = 531)

Characteristics	Number	Percent
Gender		
Male	411	77.4
Female	120	22.6
Age (mean ± SD)	57.54±11.43	
Underlying liver disease		
Hepatitis B	273	51.4
Hepatitis C	140	26.4
Hepatitis B+C	24	4.5
Other	94	17.7
Child pugh score		
Child-A	394	73.6
Child-B	113	21.2
Child-C	24	4.5
AFP Median (min-max)	162.13 (0.54 to 116,232)	

Value are represented as number, percent (%), mean ± SD

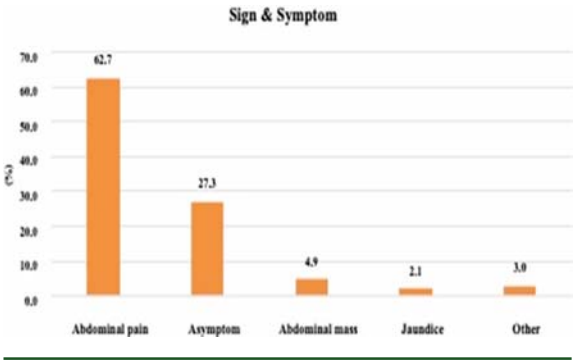

Figure 1. Clinical presentation of HCC patients in Rajavithi Hospital.

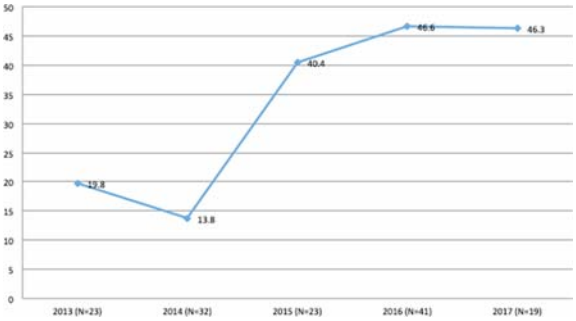

Figure 2. Resectability rate of HCC patients in Rajavithi Hospital.

Table 2. Tumor characteristics of HCC patients from 2013 to 2017 (n = 531)

Characteristics of tumor	Number	Percent
Number		
1	342	64.4
2	79	14.9
3	24	4.5
>4	86	16.2
Segment		
Right	282	53.1
Left	92	17.3
Both	153	28.8
Caudate	4	0.8
Extrahepatic metastasis	33	6.2
Vascular invasion		
Inferior vena cava	23	4.3
Portal vein	91	17.0
Hepatic vein	18	3.4

Value are represented as number and percent (%)

Table 3. Operative data of patients who underwent resection in Rajavithi Hospital (n = 138)

	Number	Percent
BCLC stage		
Stage 0	2	1.4
Stage A	40	29.0
Stage B	53	38.4
Stage C	43	31.2
Procedure		
Open hepatectomy	114	82.6
Laparoscopic hepatectomy	24	17.4
Operative time (hours)		
Open hepatectomy	3.8±1.6	
Laparoscopic hepatectomy	4.1±1.8	
Estimated blood loss (cc)	850 (300 to 9,000)	
Pringle time (minutes)	33.8±17.1	
90-day mortality rate	5	3.6

Value are represented as number, percent (%), mean ± SD, median (min-max)

patients did not receive any treatment due to having advanced disease (Figure 4).

In the present study, the overall survival rates after 1, 3, and 5 years of HCC patients who underwent resection between 2013 and 2016 were 74.0%, 60.0% and 59.4% respectively (Figure 5).

Discussion

Hepatocellular carcinoma is still a horrible disease in Thailand, and most patients who have it come to the hospital at late stages of their condition. In Asia, the leading cause of HCC is viral infection, and a number of studies have revealed that up to 50 to 70% of patients had HBV-related HCC. Surgery, whether it be liver resection or liver

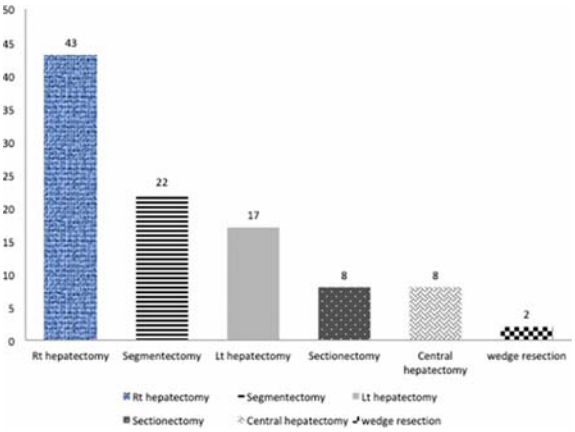

Figure 3. Operation types performed on HCC patients in Rajavithi Hospital.

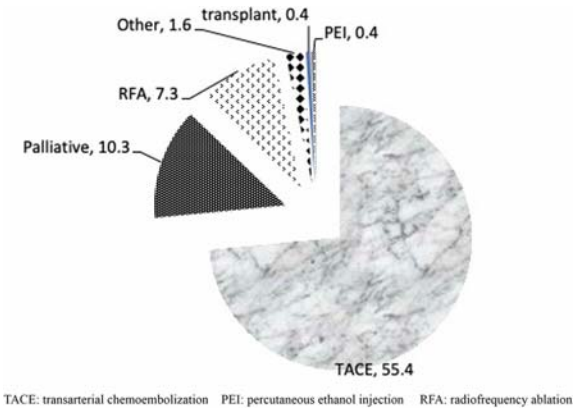

Figure 4. Other treatment modalities performed on HCC patients in Rajavithi Hospital.

transplantation, remains an effective treatment for HCC; for instance, the 5-year survival rate after hepatic resection in a recent large series was 50 to 60%, and the disease-free survival rate was 23 to 32%[5,6]. Interestingly, the 5-year survival rate in a Japanese group[6] was higher at over 70%, while the rates of survival of patients who underwent liver transplant was 80%.

Our data showed that the most common cause of HCC was HBV infection, and this concurs with the results of other studies in Asia, where resectability rates are showing an upward trend, increasing from 20% to 46%. In our study, patients who underwent operation while in the early stage of the disease accounted for only 1.4% of cases, while 29.0% of patients were in stage A including those with multifocal tumor <3 tumors and single tumor 2 to 5 cm, and 69.6% were in intermediate stages associated with tumors greater than 5 cm and vascular involvement.

The treatment modalities in the intermediate stages are quite limited. According to BCLC guidelines, TACE is

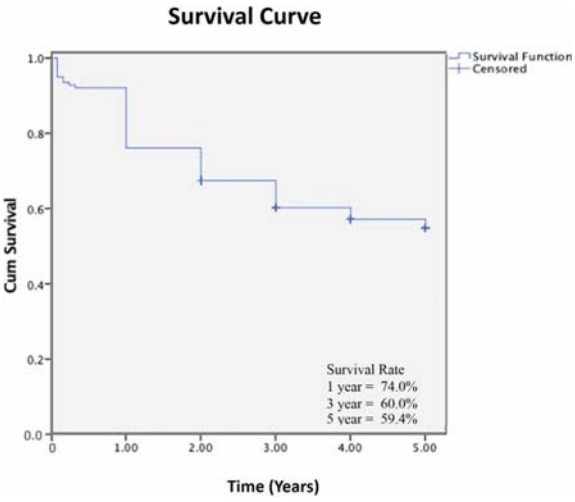

Figure 5. Survival rates of HCC patients who underwent resection.

the best option in this stage, but in Asia, liver resection is widely offered to patients with multifocal, bilobar tumors or tumors with vascular invasion. Studies from China[7] have revealed that when liver resection was used for patients with multinodular HCCs, both the 3-year and 5-year survival rates were better in patients who underwent resection than those who had TACE (63.5% and 51.5% vs. 35% and 18% respectively, with median post-operative morbidity of 25%, and 90-day mortality of 2.7%. In another study, patients with macrovascular invasion who underwent hepatic resection had median postoperative morbidity of 33% and in-hospital mortality of 2.7%. Median survival was 15 months, and the 3- and 5-year survival rates were 33% and 20% respectively. Three similar retrospective[8,9,11] studies compared liver resection with other treatments, such as local ablation, TACE, and Sorafenib, and found that the liver resection group had better overall survival. In a recent systematic review[10] looking at conservative treatments (Sorafenib, hepatic arterial infusion chemo-therapy, TACE, RFA, and combinations) for patients with portal vein tumor thrombus (PVTT), the median survival ranged from 4.4 to 12.5 months.

Currently, laparoscopic hepatectomy has largely acceptable outcomes, but our study used it in only 17.4% of cases, as it has limitations relating to larger-sized tumors and the presence of vascular invasion. Operative time is similar in open and laparoscopic hepatectomy. Our 90-day mortality rate was slightly higher and one-year survival rate a little lower than those of another study[8,9,11]; however, most of our patients presented at an intermediate stage, and this is the main factor associated with worse prognosis and reduced survival. The limitations of this study were its retrospective nature and the fact that we did not evaluate morbidity, disease-free survival and long-term survival.

In the Thai context, there are many limiting factors. Liver resection remains the treatment of choice for patients with HCC, as it offers increased long-term survival and improved quality of life. Patient selection before the operation is crucial in achieving better results; in particular, intermediate-stage biological behavior tests should be considered.

Conclusion

In conclusion, HCC is a fatal complication in patients with chronic liver disease. Chronic HBV infection is a significant risk factor for HCC among Thai patients, most of whom present at a late stage, resulting in inferior longterm outcomes.

Although there have been advances in several modalities employed for treatment of HCC, the single most effective strategies for improved survival rates are prevention of HBV transmission and early detection of HCC. When patients are at high risk of developing HCC, it is important to strictly adhere to the screening policy.

What is already known on this topic?

Resectability rates are increasing in the modern era, but the overall outcomes in Thai patients remain inferior because patients usually present in late stages of the disease.

What this study adds?

Background data of the patients are presented, together with resection and survival rates after hepatectomy in this tertiary care center.

Potential conflicts of interest

The authors declare no conflicts of interest.

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