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Original Article

Is lobectomy an effective treatment method in giant hepatocellular carcinomas?

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Abstract

Aim: Hepatocellular carcinomas (HCC) are diagnosed at a high frequency worldwide. The most effective treatment method is surgery. Surgical treatment of giant HCCs (HCCs ≥10 cm in diameter) remains controversial due to its advanced stage. In this study, we discuss the surgical treatment of patients with HCC with a tumor size ≥10 cm, as well as early complications and effect on survival.

Materials and Methods: Patients who underwent surgical treatment for HCC in our clinic between 2011 and 2021 were retrospectively reviewed. Patients older than ≥18 years of age who were treated with anatomical lobectomy and whose files were not missing any data were included in the study. Demographic characteristics, surgery and pathology reports, and survival data of the patients were analyzed.

Results: A total of seven patients, five of whom were men, were included in the study, and the median age was 66 years (range 28–76). The median tumor diameter was 20 cm (range 10.5–24). Anatomical lobectomy was performed in all patients. The median duration of hospitalization was 4 days (range 3–7). Perioperative morbidity and mortality were not observed. At least one liver recurrence was observed in all patients during follow-up. Pulmonary metastasis was detected in two patients during follow-up. The median survival was 24 months (range 7–60).

Conclusion: We think that lobectomy can be applied with low perioperative morbidity and mortality in patients with selected giant HCCs in experienced centers such as our clinic.

Keywords: Hepatocellular carcinoma; liver; lobectomy; metastasis; surgery

INTRODUCTION

Hepatocellular carcinoma (HCC), the most common type of primary liver cancer, accounts for 7% of all cases of cancer globally. Its incidence increases with age and is highest in patients around the age of 70 (1). Cirrhosis is found in 80%–90% of patients with HCC at the time of diagnosis (2). Since difficulties with tumor size, location, number, vascular and extrahepatic involvement, presence of cirrhosis, and insufficient liver reserve are frequently observed, only a small number of patients (<20%) may be eligible for resection and transplantation. For the remaining patients, the best option is interventional therapies (3). Unfortunately, these patients have a high rate of postoperative tumor recurrence, which significantly reduces their long-term survival (4). In some studies, HCCs with a diameter of ≥10 cm have been defined as giant HCCs (5-7). Because giant HCCs are often thought to be at an advanced stage at the time of diagnosis, treatment involving resection is still controversial (8).

In this study, we aim to review the applicability of anatomic lobectomy in patients with HCC with a tumor size ≥10 cm by determining the contribution of the treatment to survival, early complications, and the effect on overall survival.

MATERIALS and METHODS

Ethics committee approval for this study was obtained from Başkent University (project number KA21 / 217). The medical records of patients who underwent surgical treatment for HCC in our clinic between 2011 and 2021 were retrospectively reviewed. Patients who were treated by mass excision, who were younger than 18 years of age at the time of treatment, or whose files lacked data were excluded from the study. Patients aged 18 years or older who were treated with anatomical lobectomy and who did not lack data were included in the study. Age, gender, complaint, history, family history, alpha-fetoprotein (AFP) value, Barcelona clinic liver cancer (BCLC) and Child-Pugh scores, mass and other results from contralateral lobe

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thick needle biopsy, preoperative treatment and operation information, intraoperative bleeding, pathology report, hospitalization period, reoperation, additional treatment, recurrence, metastasis, and survey information were recorded and analyzed. In statistical analysis, quantitative variables are expressed as median and minimum-maximum. Descriptive statistics of qualitative variables are reported as frequency distributions.

RESULTS

A total of seven patients (two female and five male patients) were included in the study. The median age of the patients was 66 years (range 28–76). Four patients presented with abdominal swelling and one patient presented with spontaneous intra-abdominal bleeding. Two patients had no active complaints, and the diagnosis was made upon detection of a mass on examinations. There was no feature presenting symptoms in one patient's history. Two patients had a history of treatment for hepatitis B and one patient had been treated for bladder cancer. Four patients had a history of smoking and/or alcohol use. Only one patient had lung cancer in their family. The median AFP value was 154 ng/mL (range 1.3–331,000). Two patients had a BCLC score of B, and five patients had a score of C. Only one patient had a Child-Pugh score of B, while the others had a score of A.

Table 1. Characteristic of all patients

Age	45	28	53	70	66	76	73
Gender	Male	Female	Male	Male	Male	Female	Male
Symptom	Mass	Mass	Mass	None	Pain	Mass	None
Background	-	Cigarette	Alcohol	Bladder Cancer	Cigarette HBV	Cigarette Alcohol	HBV
Family history	-	Father Lung Ca	-	-	-	-	-
AFP	42600	1,3	154	8,3	331000	19636	8,3
BCLC	C	C	C	B	C	C	B
Child-Pugh	A	A	A	A	B	A	A
Tumor biopsy	-	HCC	HCC	-	-	-	-
Contralateral lobe biopsy	Cirrhosis	Normal	Normal	-	-	-	-
Preoperative treatment	Right portal vein embolization	-	-	-	-	-	-
Operation	Right	Right	Left	Left	Left *	Left	Left
Inraoperative bleeding (ml)	1000	900	330	330	660	50	50
Pathology							
Differentiation	Moderate	Moderate	Moderate	Moderate	Low	Low	Moderate
Tumor size (cm)	20	24	20	10,5	20	18	11
Tumor rupture	-	-	-	-	+	-	-
Satellite lesion	+	+	+	+	+	+	+
Invasion							
Capsula	-	-	-	-	+	-	-
Vascular	-	+	+	+	+	+	+
Lymphatic	+	+	+	+	+	-	-
Perineural	-	-	-	+	-	+	-
Cirrhosis	+	-	-	+	+	+	+
Surgical border	-	-	+	-	-	-	-
Hospital stay (days)	3	6	4	3	7	7	3
Recurrence	2	1	2	1	1	1	1
Reoperation	2	-	-	-	-	-	-
Additional treatment	TACE+ RF+CT	CT	TACE+CT	-	CT	CT	-
Metastasis	-	Lung LN	-	-	Lung	-	-
Survival (month)	60 Live	32 exitus	44 exitus	24 exitus	8 exitus	7 exitus	22 exitus

BCLC: Barcelona Clinic Liver Cancer Group, HCC: hepatocellular cancer, HBV: Hepatitis B Virus, Ca: Cancer, AFP: alpha-fetoprotein, TACE: transarterial chemoembolization, RF: radiofrequency ablation, KT: chemotherapy, LN: intra-abdominal lymph node
*Partial diaphragm excision + partial stomach and small intestine resection in addition to lobectomy

Two patients underwent thick needle biopsy of the mass, and the result revealed a diagnosis of HCC. Three patients underwent a thick needle biopsy of the contralateral lobe to determine the presence of cirrhosis, and only one of the lobes biopsied contained cirrhotic parenchyma. Only the patient with cirrhotic parenchyma received preoperative treatment (right portal vein embolization). This patient was operated on after the left lobe volume was measured at 540 cc 30 days after the procedure. Anatomical lobectomy was performed in all patients, and two of the lobes were found to be right, while the other five were found to be withered. For the patient who presented with spontaneous intra-abdominal bleeding, partial diaphragm excision and partial resections of the small intestine and stomach were also performed. The median volume of intraoperative bleeding was 330 mL (range 50–1000). The specimen pathology was reported as HCC for all patients, and the tumor was moderate in five patients and poorly differentiated in two patients. The median tumor diameter was 20 cm (range 10.5–24). Only one patient had capsule invasion with tumor rupture. The specimens of all patients had satellite lesions. Vascular invasion was present in all but one patient. Lymphoinvasion was observed in all but two patients, while perineural invasion was present in only two patients. Five patients' specimens revealed cirrhosis in the parenchyma. The surgical margin was reported as positive in only one patient. The median length of hospitalization was 4 days (range 3–7). At least one liver recurrence was observed during the follow-up in all patients. Re-operation was performed twice due to local recurrence in only one patient, who received radiofrequency ablation (RF) and transarterial chemoembolization (TACE). For the other patient who had a recurrence of the tumor twice, only TACE was applied. Five patients received postoperative chemotherapy. During follow-up, metastasis to the lung and intra-abdominal lymph nodes were observed in one patient, and lung metastasis only was observed in another patient. Only one patient was alive at the 60-month follow-up. The median survival since surgery was 24 months (range 7–60) (Table 1).

DISCUSSION

The average age at diagnosis of HCC in the United States is 65, and it has been reported to be more common in men, who comprise 74% of patients. However, the incidence of HCC occurrence is increasing in the younger population due to cases developing as a result of cirrhosis due to alcohol (9). Consistent with the literature, two of the patients in this study were women and five were men, and the median age was 66 years (range 28–76).

HCC may present with different clinical features. Some patients are completely asymptomatic, and most do not have any symptoms specific to the tumor (10). HCC is usually detected incidentally during ultrasound examination or during clinical diagnosis of liver failure (11). Generally, those with advanced disease may experience abdominal pain, weight loss, and early satiety. In some patients, a mass may be noticed in the right upper quadrant of the abdomen (10). Four of the patients in this study presented with abdominal swelling, and one patient presented with spontaneous intra-abdominal bleeding. Two of our patients had no active complaints, and their diagnosis was made upon detection of a mass during an examination.

HCC is among the cancers with increasing frequency. It is known that hepatitis B and C play a role in the etiology of 80% of the cases. Alcohol use is the second-most common cause of HCC (12). Two patients had a history of hepatitis B and four patients had a history of smoking and/or alcohol use. According to the American Liver Disease Research Association guidelines, effective and recommended treatments for HCC are surgical resection, transplantation, and percutaneous RF ablation (13).

The BCLC staging system uses in patients with HCC and underlying cirrhosis (14). Palliative and ablative procedures are recommended as patients with Stage B and C are considered to be in advanced stages. In our study, the BCLC score of two patients was B and the score of five patients was C. Portal embolization was required preoperatively in only one of these patients, and direct lobectomy was performed in the others.

Major liver resections can be performed in patients without cirrhosis due to the high regeneration capacity of the residual liver tissue. In these patients, perioperative mortality is reported to be below 1%, and morbidity is below 15% (15). When more than 25% of liver tissue is remaining in patients without cirrhosis and more than 50% is remaining in patients with cirrhosis, patients can tolerate the procedure after resection (16). It has been reported that the portal vein of the lobe to be resected can be embolized in order to avoid insufficiency in these patients, and the size of parenchyma may increase by 61% by 37 days post-resection in 80% of the patients (17). Preoperative right portal vein embolization was performed in a patient with cirrhotic parenchyma who was included in this study. This patient was operated on after the left lobe volume was measured as 540 cc 30 days after the procedure.

Hepatic resections are thought to be a safe and effective approach, especially in the treatment of uninodular HCC and HCC greater than 10 cm (8). Typical complications of liver resection include liver failure, bleeding, and bile leakage (18). No perioperative complications were observed in the seven patients on whom we performed lobectomy. During liver resection, attention should be paid to blood loss. In particular, blood loss of more than 1,000 mL, administration of blood transfusion, hypotension, prolonged operation time, prolonged hepatic blood flow occlusion, and vascular reconstructions increase the incidence of postoperative liver failure (19). In our study, the median volume of intraoperative bleeding was 330 mL (range 50–1000). It has been reported that the average hospital stay is 8 days after hepatectomy, most of which are performed due to malignancy (20). In our study, the median duration of hospitalization was 4 days (range 3–7).

Extrahepatic spread is present in more than 15% of HCC cases at the time of diagnosis and is more common when the primary tumor is greater than 5 cm in diameter. HCC most frequently metastasizes to the lungs, but can also metastasize to the intra-abdominal lymph nodes, bones, adrenal glands, and, rarely, to the brain (21). One patient in this study had neighboring organ metastases at the time of diagnosis, and partial diaphragm excision and partial resections of the small intestine and stomach were performed in addition to lobectomy. At least one liver tumor recurrence was observed in all patients during follow-up. One patient developed metastases in the lung and intra-abdominal lymph nodes, and another patient developed only lung metastasis. Post-recurrence re-excision, ablative treatments (RF, microwave ablation, cryotherapy), transverse radioembolization (TARE), TACE, and liver transplantation can be performed in eligible patients (18). Among patients in this study, re-operation was performed in only one patient at two different times due to local recurrence, with RF ablation and TACE being performed. In one patient, only TACE was performed after recurrence. The three-month major morbidity and mortality rates after hepatectomy have been reported to be 16.5% and 4.4%, respectively (20). Morbidity and mortality rates in HCC patients with a tumor diameter of 10 cm have been reported to vary between 25% and 50% and between 0% and 8%, respectively (6,7,22) In our study, patients without perioperative morbidity and mortality were discharged without issue. Other studies have reported that the median survival after resection in HCC patients with tumor diameter of 10 cm is 30–32 months (6,7,22). After large (median 10 cm) HCC resection, the 5-year mean survival is 30.3%. In many studies, hepatic resections for giant HCC are recommended by most published series because they can provide acceptable long-term survival (8). In the follow-up of the patients in this study, only one of the patients survived with illness at 60 months post-resection, and the other patients had died by this time. The median survival was 24 months (range 7–60). In our study, the mean survey was found to be lower than the literature due to the small number of patients, the need for large organ resection in a patient with perforation, tumor recurrence in the liver in all patients, and lung metastasis in two patients.

LIMITATIONS

Our study has limitations, such as the small number of patients and that a control group was not included. Nevertheless, we think that the outcomes of these surgeries performed in patients with giant HCC without perioperative morbidity and mortality will contribute to the literature.

CONCLUSION

HCC remains associated with low survival despite the availability of effective treatment. We think that lobectomy is a method that can be applied with low perioperative morbidity and mortality in patients with selected giant HCC in experienced centers such as our clinic.

Competing Interests: The authors declare that they have no competing interest.

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Ethical Approval: Ethics committee approval for this study was obtained from Baskent University (project number KA21 / 217).

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