

CLINICAL STUDY

Surgical treatment of hepatocellular carcinoma

Laca L, Dedinska I, Miklusica J, Janik J, Palkoci B, Pindura M

Surgery Clinic and Transplant Center, Jessenius Faculty of Medicine Comenius University and University Hospital Martin, Martin, Slovakia. laca_1@hotmail.com

ABSTRACT

The incidence of hepatocellular carcinoma (HCC) in Europe and throughout the world is currently increasing. This is caused by an increase in the number of patients with alcoholic liver damage, metabolic syndrome, and by increasing incidence of hepatitis B and C.

From January 1, 2004 to December 31, 2013, resection or radiofrequency ablation of the liver was done in 360 patients with benign lesions or malignant tumors of the liver. In 28 patients HCC was diagnosed and histologically confirmed (7.8 %). Seven patients had HCC associated with liver cirrhosis (25 %), and 21 patients were without histologically confirmed cirrhosis (75 %). R0 resection was done in 18 (64 %) patients.

Surgical complications occurred in 6 (21 %) patients and reoperation due to tumor relapse or progression was done eight times in 6 (21 %) patients. One-year and five-year patients' survivals were 64 % and 10 %, respectively, and did not statistically differ from the survival of the whole set of patients with tumor diseases in the given time period.

In the future it will be possible to improve the long-term survival of patients with HCC by using screening methods for presymptomatic diagnosis of HCC, precise preoperative diagnosis and efforts for R0 resection (Tab. 1, Fig. 4, Ref. 11). Text in PDF www.elis.sk.

KEY WORDS: hepatocellular carcinoma, resection treatment, survival after resection

Introduction

The incidence of hepatocellular carcinoma (HCC) in Europe and throughout the world is currently increasing. This is caused by an increase in the number of patients with alcoholic liver damage, metabolic syndrome and by increasing incidence of hepatitis B and C. At present, it is very important to monitor mainly the group of patients with nonalcoholic steatohepatitis caused by metabolic syndrome and patients with diabetes mellitus type 2 associated with obesity because even without the presence of cirrhosis in this group there is an increased risk of HCC development, (1). Curative treatment of HCC is currently possible only in 30–40 % of cases (2). Radical resection, transplantation, and radiofrequency ablation (RFA) of the liver are the only therapeutic methods that can cure the patient. Even though the survival is modified by the natural survival curve, the results of surgical treatment are good in older age groups even over 70 years, (3). This kind of treatment is however possible only in 13–35 % of patients. In other patients, the advanced state of the disease and its diffuse character does not allow such procedure.

Materials and methods

From 1/1/2004 to 31/12/2013, the Surgery Clinic of JFMED CU and UHM in Martin carried out resections or radiofrequency

ablations of the liver in 360 patients with benign lesions or malignant tumors of the liver; the average age at the time of operation was 59 years \pm 12. HCC was diagnosed and histologically confirmed in 28 patients (7.8 %) at average age of 63 years \pm 9.6 ($p = 0.0861$). Age stratification is shown in Figure 1.

Seven patients had HCC associated with liver cirrhosis (25 %), 21 patients were without histologically confirmed cirrhosis (75 %), out of which 14 patients were without any pathology, and 7 patients had steatosis, steatofibrosis or steatohepatitis in liver parenchyma. Nineteen patients were diagnosed with a solitary tumor of size from 5 to 17 cm, 7 patients had 2–5 nodules and 2 patients had more than 5 nodules. The average number of nodules per patient was 1.75. Patients with cirrhosis underwent 1 resection of more

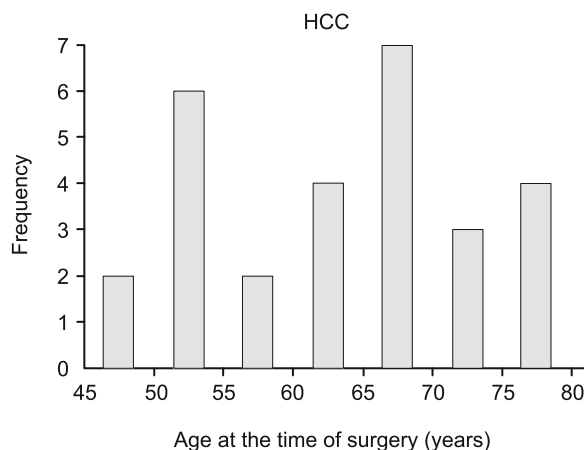


Fig. 1. Age of patients at the time of operation.

Surgery Clinic and Transplant Center, Jessenius Faculty of Medicine Comenius University and University Hospital Martin, Martin, Slovakia

Address for correspondence: I. Dedinska, MD, PhD, Dept of Surgery and Transplant center JLF UK and UNM Martin, Kollarova 2, SK-036 59 Martin, Slovakia.

Tab. 1. Distribution of the set of patients per type of resection.

Type of resection	Patients with liver cirrhosis n=7	Patients without liver cirrhosis n=21	p
Large	1 (14.3 %)	14 (66.7 %)	0.0473
Small	4 (57.1 %)	5 (23.8 %)	0.2433
Non-anatomic	2 (28.6 %)	1 (4.8 %)	0.2909
RFA	2 (28.6 %)	1 (4.8 %)	0.2909

than three segments (large), 4 resections of less than 3 segments (small), and 2 patients had nonanatomic resection. Fourteen large anatomic resections, 5 small anatomic resections, and 1 nonanatomic resection were performed in patients without cirrhosis. RFA was carried out in 2 patients with cirrhosis, and in 1 patient without cirrhosis (Tab. 1).

Statistical analyses were used as follows: Student’s t-test, Chi-square test, and Kaplan-Meier curves of survival (certified statistical program MedCalc version 13.1.2). We regard p value < 0.05 as statistically significant.

Results

Resection of the liver was done in 25 patients, R0 resection in 18 patients, R1 resection in 3 patients, and R2 resection in 3 patients. Re-resection was done in 2 patients from the group of patients with R2 resection; the third patient died 3 months after operation due to dissemination of the disease. In case of patients after R1 resection, re-resection was necessary only in one patient, the other two patients have been without tumor relapse so far. Surgical complications occurred in 6 patients (21 %); it was a biliary fistula in one case, two cases with intra-abdominal abscess, 2 cases with fluidothorax requiring puncture, and in one case it was infection in the surgical wound (Fig. 2).

Reoperation due to tumor relapse or progression was done 8 times in 6 patients (21 %); there were 2 cases of resection after RFA, 3 cases of re-resection after R1 and R2 resections, 1 case of RFA after previous RFA, and 2 cases of excisions due to metas-

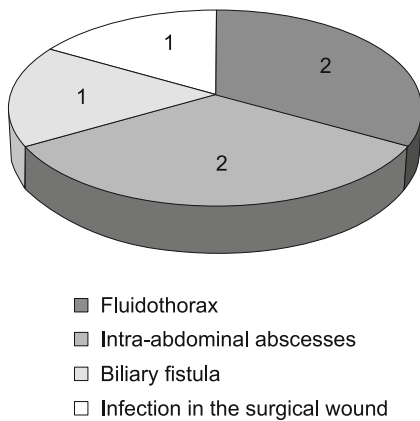


Fig. 2. Surgical complications.

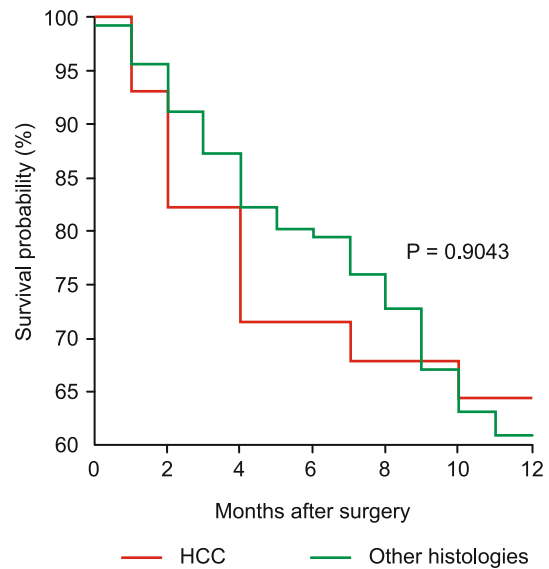


Fig. 3. One-year survival of patients with HCC and patients with tumor diseases of the liver treated at the Surgery Clinic of JFMED CU and UHM in Martin.

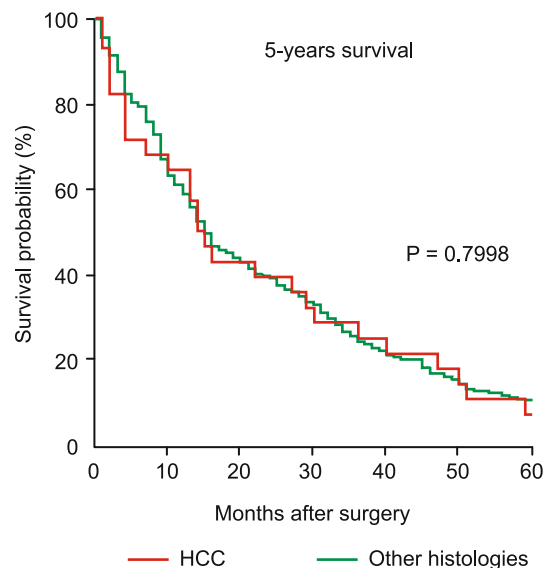


Fig. 4. Five-year survival of patients with HCC and patients with tumor diseases of the liver treated at the Surgery Clinic of JFMED CU and UHM in Martin.

tases in the surgical wound. No re-resection was done in patients with R0 resection.

One-year and five-year survivals of patients are shown in Figures 2 and 3. One-year survival was 64 %, five-year survival was 10 % in our set of patients. Survival of patients with HCC did not statistically differ from that of the whole set of patients with tumor diseases in the given time period (Figs 3 and 4).

Discussion

The current therapeutic options for the treatment of HCC according to BCLC (Barcelona Clinic Liver Cancer) group can be summed up as follows:

A) Radical surgical therapy in early stages and in case of non-cirrhotic liver or liver with Child–Pugh A and A–B cirrhosis (resection, transplantation, RFA in case of small nodules up to 2 cm and less than 3 nodules to a diameter of 3 cm in case of Child–Pugh A/B cirrhosis),

B) Palliative care in case of multinodular disease, vena portae infiltration or extrahepatic dissemination, in case of Child–Pugh AB cirrhosis chemoembolization and chemotherapy),

C) Symptomatic therapy in the terminal stage in case of Child–Pugh C (4).

Treatment of HCC depends on its early detection and level of damage of the liver parenchyma. Survival of patients who had been diagnosed with HCC during screening examination was better than in symptomatic patients (5). A randomized study of patients with chronic hepatitis B proved that owing to early detection of HCC, regular ultrasonographic checkups in these patients decreased mortality in this group from 80 % to 37 % (6). On the other hand, the examination of alpha-fetoprotein levels showed that this examination has no importance as a screening method (7). Our clinic receives patients with suspicion of HCC mainly with non-cirrhotic liver or early-stage cirrhosis. Beside cirrhosis, there are also other prognostic factors that affect patients' survival, namely listed in ascending order as follows: disease spread into vena portae, microvascular spread, number of lesions, satellite lesions, level of AFP, tumor size, age, and subjective consideration of the possibility of surgical treatment by the surgeon (8). At present, patients' survival after surgical resections has significantly increased. The five-year survival described in literature ranges from 20 % to 70 %. Surgical mortality is claimed to be below 2 % in patients without cirrhosis and up to 10 % in cirrhotic patients. The fibrolamellar variant of HCC has long been considered to be a tumor with a better prognosis; however, long-term studies have not proved this supposition. In case of resection therapy, there are prognostically better results only after transplantations due to HCC (9). Liver resection is a method of choice in case of resectable HCC in patients without cirrhosis or with clinically fully compensated cirrhosis according to the generally accepted Barcelona Clinic Liver Cancer (BCLC) classification. Even though there was zero mortality in our set of patients, the five-year survival was only 10 %. We explain this mainly by the advanced state of the disease at the time of admission and high average age of patients, where most patients were aged 65–80 years. The recurrence of HCC after resection treatment is high despite negative resection borders. This is explained by both occult spread of the tumor via the portal venous system, and development of a secondary tumor in the environment of cirrhosis or hepatitis. Re-resection is possible only in 10–29 % of patients, but the results are favorable and the 5-year survival is claimed to be identical to that in cases of primary resection (10). In our set

of patients, re-resection was carried out in 6 patients (21 %) due to recurrence of the disease; however, re-resection was necessary in no patient after primary R0 resection.

Conclusion

Resection treatment of HCC is still a method of choice in patients with tumors in non-cirrhotic and Child–Pugh A/B cirrhotic liver. The prognosis of the disease depends on early diagnosis and possibility of achieving R0 resection. Sonography shows to be a good screening method which also provides detection of pre-clinical stages of the disease. The MRI or three-phase CT scan examinations are dominant among the non-invasive methods (11). Liver resections in elderly patients do not increase operational mortality, but reduce the long-term survival with respect to physiological life curve. We believe that we will be able to achieve an improvement in long-term patients' survival by means of early diagnosis and increased radicalness of resections.

References

1. Ascha MS, Hanouneh IA, Lopez R et al. The incidence and risk factors of hepatocellular carcinoma in patients with nonalcoholic steatohepatitis. *Hepatology* 2010; 51: 1972–1978.
2. Germano D, Danielle B. Systematic therapy of hepatocellular carcinoma: Current status and future perspectives. *World J Gastroenterol* 2014; 20 (12): 3087–3099.
3. Nishikawa H, Kimura T, Kita R, Osaki Y. Treatment for hepatocellular carcinoma in elderly patients: A literature review. *J Cancer* 2013; 4 (8): 635–643.
4. Forner A, Reig ME, De Lopes CR et al. Hepatocellular carcinoma. 1283–1286. In: Jarnagin WR et al. *Blumgart's Surgery of the liver, biliary tract and pancreas*. Philadelphia: WB Saunders, 2012.
5. El-Serag HB. Hepatocellular carcinoma. *New Engl J Med* 2011; 365: 1118–1127.
6. Zhang BH, Yang BH, Tang ZY. Randomized controlled trial of screening for hepatocellular carcinoma. *J Cancer Res Clin Oncol* 2004; 130: 417–422.
7. Malek NP, Schmidt S, Huber P et al. Clinical practice guide line: The diagnosis and treatment of hepatocellular carcinoma. *Dtsch Arztebl Int* 2014; 111 (7): 101–106.
8. Neeff H, Makoviec F, Harder J et al. Hepatic resection for hepatocellular carcinoma – results and analysis of the current literature. *Zbl Chir* 2009; 134 (2): 127–135.
9. Bruix J, Boix L, Sala M et al. Focus on hepatocellular carcinoma. *Cancer Cell* 2004; 5 (3): 215–219.
10. Clavien PA, Lesurtel M, Bossuyt PM et al. Recommendations for liver transplantation for hepatocellular carcinoma: an international consensus conference report. *Lancet Oncol* 2012; 13 (1): 175–179.
11. Bota S, Piscaglia F, Marinelli S et al. Comparison of International Guidelines for Noninvasive Diagnosis of Hepatocellular Carcinoma. *Liver Cancer* 2012; 1: 190–200.

Received October 21, 2014.

Accepted January 25, 2015.