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Long-term results of surgery for small primary liver cancer in 514 adults

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Abstract During 1958–1993, 2030 patients with pathologically proven primary liver cancer (PLC) were retrospectively reviewed. Comparison between small PLC (~< 5 cm, n = 514) and large PLC (> 5 cm, n = 1516) revealed that small PLC had a higher resection rate (92.4% versus 49.1%), lower operative mortality (1.7% versus 5.2%), a higher percentage of single tumour nodules (78.0% versus 53.4%), a higher percentage of well encapsulated tumour (74.5% versus 35.8%) and higher survival rates after resection (5-year, 63.8% versus 36.6%; 10-year, 46.8% versus 28.5%). No significant difference was found between survival following limited resection (n = 440) and lobectomy (n = 34) in patients with small PLC. Re-resection of any subclinical recurrence or solitary pulmonary metastasis after small PLC resection was done in 70 cases. These results indicate that resection is still the modality of choice for treatment of small PLC; limited resection instead of lobectomy was the key to increasing resectability and decreasing operative mortality; re-resection of subclinical recurrence was important to prolong survival further.

Key words Hepatoma · Resection · Prognosis

Abbreviations PLC primary liver cancer · AFP α-fetoprotein · HBsAg hepatitis B surface antigen

Introduction

Primary liver cancer (PLC) is one of the world's commonest malignant neoplasms. It is most prevalent in southeast Asia and portions of Africa, and a relatively rare malignancy in the western world. Every year PLC causes 250,000 deaths in the world and 110,000 deaths in China (Zhou 1994). Recent implementation of screening programmes using α-fetoprotein (AFP) and ultrasonography in high-risk populations identified increasing numbers of patients with small PLC (~< 5 cm). Several reports have shown improved survival after limited resection for small PLC (Lee et al. 1985; Paquet et al. 1991; Tang et al. 1989; Yu et al. 1980). However, this improved survival has not been observed uniformly (Lai et al. 1991). Moreover, the clinicopathological features, operative strategy and long-term outcome for patients with these small PLC are different from those for patients with large PLC. This paper summarizes our experience with this condition over the past three decades.

Materials and methods

Patients

Between January 1958 and December 1993, a total of 2032 patients with pathologically proven PLC were admitted to the Zhong Shan Hospital of Shanghai Medical University. Of these, 514 (25.3%) were cases of small PLC (~< 5 cm), comprising 473 men and 41 women of median age 50 (21–78) years. The tumour was asymptomatic in 69.8% (359/514) and detected by AFP serosurvey and/or ultrasonography either in the natural population in the early years of the study or in a high-risk population in recent years. The criteria for the high-risk population were defined as having a history of hepatitis, liver cirrhosis and/or serum hepatitis B surface antigen (HBsAg) when aged over 40 years. A total of 155 patients (30.2%) were discovered to have clinical symptoms. In recent years, the number of small PLC has remarkably increased (Fig. 1).

The serum concentration of AFP was abnormal (> 20 ng/ml, immunoassay) in 86.2% (437/507) of the patients tested. Serum AFP
Fig. 1 Distribution of small primary liver cancer according to year

was 21–400 ng/ml in 36.8% (161/437). Serum γ-glutamyl transpeptidase (normal value below 6 units/ml, Orlowski’s method) was slightly elevated (6–12 units/ml) in 37.1% (184/496), and markedly elevated (> 12 units/ml) in 28.6% (142/496) of the patients tested. Alanine aminotransferase (normal value < 40 units/ml) was elevated in 7.4% (38/514).

The background of liver disease was as follows: 61.5% (316/514) had a history of hepatitis, of these, 84.5% (267/316) had a history lasting over 5 years coexisting liver cirrhosis occurred in 91.6% (471/514), of which 71% was macronodular cirrhosis (cirrhotic nodules of at least 0.3 cm) (330/471) and 29.9% was micronodular cirrhosis (cirrhotic nodules of less than 0.3 cm) (141/471). Serum HBsAg, assayed by reverse passive haemagglutination, was observed in 75.5% (358/474).

The positive findings for different measures of localization were as follows: angiography 85.1% (40/47), real-time ultrasonography 97.0% (453/467) and computed tomography 96.2% (331/344).

Indications for surgery included patients with compensated liver function, including serum bilirubin below 20 mg/dl, prothrombin time above 50% of the normal value, a preserved albumin/globulin ratio, no distant metastasis and a good general condition.

Surgical technique

A right subcostal incision is preferred either with an extension cranial to the xiphoid process or with a left extension in a chevron fashion for the resection of a tumour of the left lobe. Right thoracic extension is rarely used. In recent years, intraoperative ultrasound has been used to exclude previously undetected lesions or/and localize tumours situated under the liver surface and not palpable. For control of bleeding during transection of the hepatic parenchyma, temporary occlusion of the portal pedicle (Pringle’s manoeuvre) was frequently used in this series. Generally the occlusion time should not exceed 20 min for mild to moderate cirrhosis and 15 min for severe cirrhosis. Repeated occlusion was sometimes needed for a complicated resection with 3–5 min of perfusion. The raw surface of the liver is either sutured side to side to reduce the raw area and to provide a tamponade effect on the smaller vesicles, or covered with a piece of omentum or faciform ligament. Adequate drainage is important.

If resection is not indicated, various surgical modalities other than resection, including cryosurgery with liquid nitrogen, hepatic artery ligation or/and hepatic artery cannulation for chemotherapy can be employed.

Operative mortality indicates death within 30 days of the operation. Radical resection includes complete removal of the tumour, without grossly identified tumour emboli in the portal vein, and no tumour residue either in the remaining liver tissue or in the cut surface.

Follow-up

Long-term follow-up after surgery was done by measuring serum AFP and ultrasonography every 2–3 months, and chest radiography every 6 months during the first 2 postoperative years and at 6-month intervals thereafter. Computed tomography or a hepatic angiogram was done when intrahepatic recurrence was suspected. A microcomputer was used for the storage, analysis and statistical treatment of clinical data. Survival rates, excluding the 30-day postoperative deaths, was calculated according to the life-table method.

Results

Treatment (Tables 1 and 2)

The treatment modalities of 514 cases included resection in 474 cases (92.2%), various surgical operations other than resection (cryosurgery or hepatic artery ligation or/and cannulation) in 36 cases (7.0%) and conservave treatment in 4 cases (0.8%) because of uncompensated liver function and poor general condition. When compared with large PLC, small PLC had a higher resection rate (92.2% versus 49.1%, \( P < 0.001 \)), a higher radical resection rate (94.3% versus 75.0%, \( P < 0.001 \)), and a lower operative mortality (1.7% versus 5.2%, \( P < 0.001 \)). A limited resection (any kind of non-segment resection) was performed more frequently for patients with small PLC (82.9% versus 55.0%, \( P < 0.001 \)).

Reoperation for subclinical recurrence after radical resection was done in 15.7% (70/447) of the patients. The liver was the site of first recurrence in 67 patients (95.7%). Three patients (4.3%) were found to have metastatic lesions in the lung. A second hepatic resection was done in 56 patients and lobectomy for lung metastasis in 3 patients. The 1-, 3- and 5-year survival rates were 84.6%, 52.8%, and 47.3% respectively for patients undergoing resection of a recurrent tumour.