

Clinical Science

Impact of advanced age on the short- and long-term outcomes in patients undergoing hepatectomy for hepatocellular carcinoma: a single-center analysis over a 20-year period



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Abstract

BACKGROUND: The purpose of this study was to analyze the influence of age on both the risk of hepatectomy and the prognosis in patients with hepatocellular carcinoma (HCC).

METHODS: Patients undergoing an initial hepatectomy for HCC were classified into 2 age groups: 75 years or over ($n = 113$) and less than 75 years ($n = 499$).

RESULTS: A zero 90-day mortality was achieved in the elderly. Although the recurrence rate and recurrence sites were almost similar between the 2 groups, the 5-year survival rate in the elderly patients was significantly lower than that in the younger patients (46.0% vs 57.6%; $P = .018$), possibly because of the higher incidence of deaths from other causes (26.8% vs 10.4%; $P = .011$) in the elderly.

CONCLUSION: Selected elderly HCC patients can undergo a hepatectomy safely and can benefit from long-term HCC control comparable with that of their younger counterparts.

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Liver resection for the treatment of hepatocellular carcinoma (HCC) carries a substantial risk of mortality and morbidity, because a majority of the patients have impaired liver function caused by cirrhosis or chronic hepatitis. This concern is heightened in older patients because of the increasing incidence of comorbid illnesses with age, which can compromise the ability of the patients to withstand surgical stress¹ and age-associated parenchymal^{2,3} or nonparenchymal liver cell dysfunction.⁴ Similarly, comorbidity in

the elderly could be detrimental to the quality of life and even the overall survival, depending on its severity.⁵

Although single-center studies of surgical outcomes in older patients have been criticized for their inherent selection biases,^{6,7} these studies could offer valuable data, such as the profiles of postoperative events occurring beyond 30 postoperative days and the long-term outcomes. Previous single-center studies have shown that surgical resection offered comparable long-term outcomes in selected elderly patients and younger patients with HCC, without increasing the operative risks.⁸⁻¹¹ However, the significance of age on the surgical outcomes has not been fully evaluated in previous studies from the viewpoint of the resectability rate and its trend, treatment for disease recurrence, and cause of death.

The aim of this study was to evaluate, in a comprehensive manner, the impact of advanced age (75 years or over) on the short- and long-term outcomes in HCC patients undergoing hepatectomy by comparing the results with those reported for younger patients aged less than 75 years.

Methods

Patients

Between April 1990 and July 2013, a total of 926 HCC patients were referred to our department for evaluation of their suitability as candidates for surgical treatment. The patients comprised 199 patients aged 75 years or over and 727 patients aged less than 75 years. The cutoff point of 75 years was selected based on previous reports.^{12,13} Among the patients, 113 elderly patients and 499 younger patients had undergone initial and curative liver resection, and the data of these patients were compared retrospectively from the viewpoint of the short- and long-term outcomes. None of the patients in either group had received postoperative adjuvant therapy. The trend of the type of treatment employed and the overall morbidity rate were analyzed by dividing the total time period of the study into the following 2 time periods: first period: 1990 to 2001; second period: 2002 to 2013.

Indications for liver resection

The same surgical strategy for HCC was employed throughout this study period. Patients with an Eastern Cooperative Oncology Group performance status of grade 4 (completely disabled, cannot carry on any self-care, totally confined to bed or chair) were not considered as surgical candidates.¹⁴ The indications for surgical resection and the operative procedure were determined based on the presence/absence of ascites, the serum bilirubin level, and the indocyanine green retention rate at 15 minutes (ICGR15).¹⁵ The liver volume to be resected and the volume of the remnant liver after hepatectomy were calculated based on computed tomographic (CT) images,

for all patients scheduled for resection of 2 or more Couinaud's segments,¹⁶ regardless of the presence/absence of underlying liver disease. A cardiovascular consultation was requested for all patients aged 70 years or over,¹⁷ those aged less than 70 years who had abnormal findings on an electrocardiogram examination and/or a history of cardiovascular disease, and symptomatic patients. According to the The American College of Cardiology/The American Heart Association 2007 guidelines,¹⁸ the need for further cardiac evaluation was assessed and coronary revascularization using coronary artery bypass grafting or percutaneous coronary intervention was performed when appropriate. In cases with poor pulmonary function, the diffuse capacity of carbon monoxide was also assessed. After the completion of a preoperative evaluation, we decided whether to operate on a patient-by-patient basis after comprehensively considering the following points: the severity of comorbid illness, the extent of the cancer, the planned surgical procedure itself, and the risks of general anesthesia.

Surgical procedure

Intraoperative ultrasonography was performed in all cases to detect the presence of any occult tumors that may not have been detected by preoperative imaging modalities, and to confirm the spatial relationships between the tumors and vascular structures.¹⁹ Liver transection was performed using the clamp crushing method²⁰ and/or an ultrasonic dissector.²¹ Intermittent Pringle's maneuver was applied during liver transection, namely, 15 minutes of occlusion alternating with 5 minutes of reperfusion. Bleeding or bile leakage points were meticulously suture ligated. Anesthesia was maintained by reducing the tidal volume of ventilation to 30% to 40% of the standard volume and keeping the central venous pressure below 5 cm H₂O to decrease the amount of blood loss from the hepatic veins during transection. Packed red blood cell transfusion was not administered unless the hematocrit fell below 25% during surgery or to less than 20% on the day after the operation, provided that the patient's hemodynamic status remained stable.

Follow-up

After discharge, the patients were closely followed up at our outpatient clinic. All the patients underwent routine examinations for recurrences every 3 months, including ultrasonography and the measurement of alpha-fetoprotein (AFP) and des-gamma-carboxy prothrombin levels.^{22,23} Computed tomography with contrast medium was performed every 6 months. Recurrence was diagnosed when these imaging modalities showed a new lesion with typical radiologic features of HCC.²⁴ The indications for a repeat hepatectomy for recurrent HCC were basically decided in a manner similar to those used for the first liver resection.²⁵ Nonsurgical treatment, such as transcatheter arterial

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