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Trends in surgical results of hepatic resection for hepatocellular carcinoma: 1,000 consecutive cases over 20 years in a single institution

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Abstract

BACKGROUND: Surgical results have been reported to be improved in hepatic resections for hepatocellular carcinoma (HCC) in recent years, but the detailed trends in surgical results for HCC in a single high-volume center are still not clear.

METHODS: Surgical results in 1,000 hepatic resections for HCC performed at a single medical center from 1989 to 2011 were analyzed. Patients were divided into 3 groups: those performed in the early period (1989 to 1995, n = 181), the middle period (1996 to 2004, n = 391), and the late period (2005 to 2011, n = 428).

RESULTS: Hospital mortality (3.9%, 1.0%, and .5%; $P = .0027$) and morbidity (45%, 24%, and 15%; $P < .0001$) rates were significantly decreased. The overall survival rates were significantly improved (50%, 72%, and 78% at 5 years; $P = .0021$), but there was no significant difference in the disease-free survival (29%, 34%, and 31% at 5 years; $P = .7823$).

CONCLUSIONS: Surgical results of hepatic resections for HCC were significantly improved, with the mortality rate nearly reaching 0%. The 5-year survival rate after hepatic resections for HCC was also improved to 78%, but the consistently high rate of HCC recurrence after hepatic remains a problem.

Hepatocellular carcinoma (HCC) is one of the most common malignancies worldwide, with an annual occurrence of at least 1 million new cases.[1] The mainstay of curative treatment for HCC is hepatic resection. In the 1980s, hepatic resections for HCC were associated with a high mortality rate in the range of 10%.[2,3] Over the past decade, many large studies have documented better perioperative results, with operative mortality rates typically less than 2% and trending toward 0% in high-volume centers in Japan[4–6] and around 5% in other countries.[7,8] The decline in operative mortality is attributable to the improvement in

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careful patient selection,[9,10] meticulous surgical techniques,[4,5] and intensive perioperative care.[11,12]

Because of the advances in hepatic resection,[13,14] postoperative surveillance for recurrence, management of HCC recurrence, and interferon (IFN) therapy,[15,16] long-term surgical results such as the 5-year survival rates after hepatic resections for HCC have been improved and are now in the range of 50% to 60%.[17,18] Our colleges reported an improvement of 5-year survival to 70.3% in hepatitis C virus antibody-positive patients with HCC after hepatic resections over the years 2000 to 2006.[19]

The present study analyzed 1,000 consecutive patients who underwent hepatic resections for HCC from 1989 to 2011 at a single institution and clarified trends in the operative mortality, morbidity, and prognosis of patients with hepatic resection for HCC by dividing the treatment into 3 periods of 6 to 8 years each.

Methods

Patients

A total of 1,000 hepatic resections for HCC were performed at the Department of Surgery, Hiroshima Red Cross and Atomic Bomb Survivors Hospital, Hiroshima, Japan, between January 1989 and December 2011. Thirty-eight patients (.38%) received lipiodolization,[20] and 8 patients (.08%) received ablation therapy before hepatic resection. Only 1 patient (.01%) received percutaneous transhepatic portal embolization in order to perform an extended right lobectomy for HCC. In the same timeframe, 124 ablation therapies and 283 lipiodolizations[20] for HCC were performed at our department, and 2 liver transplantations for patients with end-stage liver cirrhosis and HCC were performed at the transplantation center in Japan according to our recommendation using the previously described strategy.[21] According to the changing of directors, perioperative management, and surgical techniques, this period was divided into 3 periods: the early period (1989 to 1995, n = 181), the middle period (1996 to 2004, n = 391), and the late period (2005 to 2011, n = 428). All directors at our department were trained in liver surgery at the same institution (Kyushu University, Fukuoka, Japan); therefore, the differences of the management policy for patients with HCC caused by the surgeons were thought to be minimal. The medical records of all patients were followed up; we collected patient data through March 2012. Twenty-four patients (2.4%) were lost to follow-up. The median follow-up period in this series was 52 months. This study was conducted in accordance with the Declaration of Helsinki after approval from our institutional review board.

Surgical techniques and follow-up methods

Details of the surgical techniques and patient selection criteria have been reported previously.[10,14] We considered surgical indication based on patients' activity of daily living, patients' age, fitness degree of tumor invasion, extent of resection, and remnant liver function. Simply speaking, patients with an indocyanine green dye retention rate at 15 minutes less than 40% were selected for hepatic resection, and patients with an indocyanine green dye retention rate at 15 minutes less than 35% were selected for anatomic resection.[14] Anticoagulant drugs, such as nafamostat mesilate,[11] were administered perioperatively since the middle period, and preoperative steroid administration was routinely performed during the late period.[12] Intravenous antibiotics for surgical prophylaxis were given for 3 days or more in the early and middle period and for 2 days or less in the late period.

In almost all hepatic resections, the intermittent Pringle maneuver consisting of clamping the portal triad for 15 minutes and then releasing the clamp for 5-minute intervals or hemivascular occulusion[22,23] was applied. The clump-crushing method was used to transect the liver parenchyma from the early period to the early part of the middle period, and an CUSA system (Valleylab, Boulder, CO) was used since the later part of the middle period, with the addition of a VIO soft-coagulation system (ERBE Elektromedizin, Tübingen, Germany) since 2010.[24] During the late period, hepatic venous backflow control,[25] which was typically achieved extrahepatically before dividing the liver, and the Belghiti hanging maneuver,[26] in which a tape was introduced behind the caudate lobe through the groove between the right and middle hepatic vein, were performed. An intraoperative bile leakage test has been routinely performed during the late period.[27]

Five surgical outcomes were mainly examined: postoperative mortality, morbidity, duration of hospital stay, overall survival, and disease-free survival. Any death that occurred in the hospital after operation was recorded as a mortality. Complications such as liver failure, encephalopathy, gastrointestinal bleeding, intraperitoneal abscess, abdominal hemorrhage, bile leakage, pleural effusion, intractable ascites, and wound infection were evaluated using the Clavien-Dindo classification[28] of surgical complications, and a grade of II or more, which required pharmacologic treatment with drugs or invasive surgical/endoscopic/radiologic interventions, was defined as positive. After discharge, all patients were examined for recurrence by ultrasonography and tumor markers such as α-fetoprotein and des-γ-carboxy prothrombin every month and by dynamic computed tomographic imaging every 3 or 4 months.[17] No patients received adjuvant chemotherapy or adjuvant lipiodolization at our institution. We treated recurrent HCC with repeat hepatectomy,[29] ablation therapy, and lipiodolization according to the previously described strategy.[30]

Statistical analysis

Continuous variables were expressed as means ± standard deviation and compared using an analysis of variance test. Categorical variables were compared using either the chi-square test or the Fisher exact test as appropriate. Survival curves were generated by the Kaplan-Meier