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Oncologic superiority of anatomic resection of hepatocellular carcinoma by ultrasound-guided compression of the portal tributaries compared with nonanatomic resection: An analysis of patients matched for tumor characteristics and liver function

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ABSTRACT

Background: The superiority of anatomic resection compared with nonanatomic resection for hepatocellular carcinoma remains a matter of debate. Further, the technique for anatomic resection (dye injection) is difficult to reproduce. Anatomic resection using a compression technique is an easy and reversible procedure based on liver discoloration after ultrasound-guided compression of the tumor-feeding portal tributaries. We compared the oncologic efficacy of compression technique anatomic resection with that of nonanatomic resection.

Methods: Among patients with resected hepatocellular carcinoma, patients who underwent compression technique anatomic resection were matched 1-to-2 with nonanatomic resection cases based on the Child-Pugh class, Model for End-Stage Liver Disease score, cirrhosis, hepatocellular carcinoma number (1/>1), and hepatocellular carcinoma size (>30, 30–50, and >50 mm). The exclusion criteria were nonanatomic resection because of severe cirrhosis, major hepatectomy, 90-day mortality (0 compression technique anatomic resection), non–cancer-related death, and follow-up <12 months. A total of 47 patients who underwent compression technique anatomic resection were matched with 94 nonanatomic resection cases.

Results: All patients were Child-Pugh A, and 53% were cirrhotic. Liver function tests and signs of portal hypertension were similar between the groups. There was 1 hepatocellular carcinoma in 81% of the patients, and the hepatocellular carcinoma was ≥30 mm in 68%. Patients undergoing anatomic resection with compression had better 5-year survival (77% vs 60%; risk ratio = 0.423; $P = .032$; multivariable analysis), less local recurrences (4% vs 20%; $P = .012$), and better 2-year local recurrence-free survival (94% vs 78%; $P = .012$). Nonlocal recurrence-free survival was similar between the groups. The compression technique anatomic resection group more often had repeat radical treatment for recurrence (68% vs 28%; $P = .0004$) and had better 3-year survival after recurrence (65% vs 42%; $P = .043$).

Conclusion: Compression technique anatomic resection appears to provide a more complete removal of the hepatocellular carcinoma–bearing portal territory. Local disease control and survival are better with compression technique anatomic resection than with nonanatomic resection.

Introduction

Liver resection is a potentially curative treatment for hepatocellular carcinoma (HCC).[1–3] In selected patients with adequate liver function, resection is even the first-line treatment option.[4–7] Recent application of laparoscopic liver resection appears to have expanded the role for operative treatment in HCC patients.[8]

The most appropriate technique for resecting HCC remains a matter of debate. HCC tends to spread along portal branches, and microsatellites can be detected in the tumor-bearing portal territory.[9,10] A *de principe* anatomic resection (AR) of the HCC-bearing portal territory is therefore recommended but has been poorly adopted for 2 main reasons. First, there is controversy about

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whether AR is superior to nonanatomic resection (NAR).[11–16] Second, performing a true AR is technically demanding because the HCC-bearing portal territories are irregular and an HCC can be nourished by multiple pedicles from different liver segments.[17,18] Currently the standard technique relies on the injection of blue dye into the Glissonean pedicles to outline parenchyma supplied by that vascular inflow.[10] This is a complex procedure that is rarely used in Western countries.

In 2004, Torzilli et al[19] proposed an alternative procedure termed "compression technique" that was based on intraoperative ultrasonography (IOUS).[20] After identification of the tumor-feeding portal pedicle, blunt, transparenchymal compression is applied between the surgeon's fingertip and the IOUS probe to create vascular occlusion, which results in discoloration of the downstream portal territory. This technique is easy to perform, reversible, and repeatable (offering major advantages compared with any other previously reported approach[10,21,22]), but its oncologic efficacy has never been analyzed. Accordingly, the present study analyzed the oncologic outcomes of AR for HCC performed using a compression technique (c-AR) and compared c-AR with NAR.

Methods

Patients

All 354 consecutive patients who underwent liver resection for HCC between 2004 and 2015 at our institution were reviewed retrospectively for inclusion in the study. The exclusion criteria were as follows: major hepatectomy, AR with extraparenchymal ligation of the Glissonean pedicles, thrombosis of the first- or second-order portal branches or the trunk of hepatic veins, patients with 90-day mortality (0 among c-AR patients), non–cancer-related death, and follow-up <12 months. A total of 217 patients were eligible for the analysis, including 63 c-AR patients and 154 NAR patients. In the latter group, 5 patients underwent NAR because of the severity of their cirrhosis and were excluded.

The c-AR patients were matched 1-to-2 with NAR patients based on the most relevant predictors of outcome according to the literature[1,3,4]: Child-Pugh class (A/B), Model for End-Stage Liver Disease (MELD) score (≤10 or >10), cirrhosis, number of separate HCC tumors (≥1), and size (>30, 30–50, and >50 mm). For each patient undergoing c-AR (case), the authors identified all the patients undergoing NAR having exactly the same characteristics (potential controls, same characteristics of the case in terms of tumor number and size, Child-Pugh score, MELD score, and cirrhosis). Among the identified NAR patients, 2 were randomly assigned as controls. Only cases and controls with exact matching of all the variables were retained for the analysis. If no perfect match was available, the case was excluded. Sixteen c-AR patients did not have suitable NAR patient matches. Available studies about the same topic using a propensity score matching technique reported a similar proportion of patients excluded from the analysis because of the impossibility to obtain an adequate matching.[12–16] Finally, 47 c-AR patients were matched with 94 NAR patients. This study was approved by our local ethics committee.

Preoperative patient management

The preoperative assessment of these patients with HCC was reported previously.[23,24] Preoperative tumor staging included α-fetoprotein level, abdominal computed tomography, and hepatic magnetic resonance imaging. All the patients underwent multidisciplinary evaluation before operation and after the study began. Liver transplantation was considered systematically, but patients with a single HCC and preserved liver function were preferentially scheduled for operative resection. Only patients who were deemed eligible for complete operative resection were considered for resection. Patient selection was based on general health, liver function, and the presence of portal hypertension (assessed by endoscopy). The selection criteria were as follows: performance status 0–1, American Society of Anesthesiologists score I–III, absence of ascites and encephalopathy, total serum bilirubin level <2 mg/dL, normal prothrombin time, and platelet count $>50 \times 10^3/mm^3$. In recent years, serum cholinesterase levels and transient elastography have been used to refine patient selection.[24] Esophageal varices were not a contraindication once endoscopic eradication was accomplished.[23] After resection, follow-up was performed every 3 months and included α-fetoprotein levels and abdominal ultrasonography, computed tomography, or magnetic resonance imaging.

Operative strategy and definition of AR

AR was the standard treatment for HCC patients. Patients having the following conditions were scheduled for NAR: severe cirrhotic changes, including liver incompressibility or impaired liver function (these patients were excluded from the present study); an NAR as a unique, parenchyma-sparing alternative to major hepatectomy[20]; peripherally located HCC; and the inability to identify the tumor-bearing portal territory because of multiple feeding pedicles.

The IOUS-guided, parenchyma-sparing approach was performed systematically as described previously.[20,25,26] In the c-AR group, the tumor-bearing portal pedicle was identified by IOUS and compressed transparenchymally between the probe and the surgeon's fingertip. The discolored area was marked using electrocautery. If the area did not include the entire tumor, additional tumor-bearing pedicles were identified and compressed. When direct pedicle compression was not possible because of tumor mass or hepatic vein interposition or was contraindicated (tumor thrombus), countercompression of contiguous pedicles was performed to obtain demarcation of the anatomic area to resect. Up to June 2007, the c-AR technique was used for HCC in segment 2 or segment 3. From July 2007, this technique was extended to HCC in all the liver segments.[27]

The resection was considered anatomic if the following 3 conditions were met: adequate identification (compression or countercompression) of the resection area; exposure of the vascular landmarks of the segment (hepatic veins); and ligation of the Glissonean pedicles at their origin. If subsegmentectomy was performed, liver discoloration and ligation of the pedicle at the level of compression were required.

Statistical analyses

Patients were identified in a prospectively maintained database and analyzed retrospectively. Chronic liver disease was staged and graded according to the Ishak score.[28] Morbidity included all postoperative complications and was graded using Dindo-Clavien classification.[29] Postoperative liver failure was defined according to the International Study Group of Liver Surgery definition.[30] Bile leak was defined as a bilirubin concentration in the drainage fluid >10 mg/dL on postoperative day 5 or 7.[31] Resection was classified as R1 when the operative margin was <1 mm, except for vascular detachment at segmental boundaries.[19,25,26] Local recurrence was defined as recurrence on the cut surface after c-AR or NAR or recurrence in the residual, tumor-bearing portal territory after NAR.

Categorical variables were compared using the χ^2 or Fisher exact test. Continuous variables were compared using the unpaired t test or Mann-Whitney U test. The Kaplan-Meier method was used to estimate survival probabilities, which were compared using the

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