Comparison of Outcomes of Hepatic Resection and Radiofrequency Ablation for Hepatocellular Carcinoma Patients with Multifocal Tumors Meeting the Barcelona-Clinic Liver Cancer Stage A Classification

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BACKGROUND: Although hepatic resection (HR) has been recommended as the first-line treatment option for patients with a solitary tumor, the first-line treatment for patients with multifocal tumors meeting the Barcelona-Clinic Liver Cancer (BCLC) stage A still remains unclear. This study compared outcomes for patients with multifocal tumors meeting the BCLC stage A treated by HR and radiofrequency ablation (RFA).

STUDY DESIGN: A total of 384 consecutive patients with multifocal tumors meeting the BCLC stage A, who underwent HR (n = 224) or RFA (n = 160), were included. Moreover, propensity score-matched patients were analyzed to adjust for baseline differences.

RESULTS: The 1-, 3-, and 5-year overall survival (OS) rates after HR and RFA were 96%, 71.7%, and 36.3%, and 90.0%, 72.7%, and 37.8%, respectively (p = 0.609); HR provided significantly better recurrence-free survival (RFS) rates than RFA at 1, 3, and 5 years (87.5%, 53.1%, and 20.1% vs 83.1%, 34.0%, and 9.7%, respectively, p = 0.001). Patients selected in the propensity-matching model showed similar results. Subgroup analysis also showed that HR was associated with better RFS than RFA for patients with 2 tumors, multifocal tumors located in the same lobe (Couinaud's segmentation) and segment (Takasaki's segmentation). Multivariate analysis revealed that 3 tumors, portal hypertension, and tumors located in different segments (Takasaki's segmentation) are independent predictors of poor prognosis in patients with multifocal tumors meeting the BCLC stage A.

CONCLUSIONS: For patients with multifocal tumors meeting the BCLC stage A, HR may offer significantly better RFS than RFA, and HR may be considered as the first-line treatment option for those patients. (J Am Coll Surg 2015;■:1−11. © 2015 by the American College of Surgeons)

Barcelona-Clinic Liver Cancer (BCLC) stage A is defined in patients presenting a single tumor of more than 2 cm or 3 nodules of less than 3 cm in diameter, Eastern Cooperative Oncology Group (ECOG)-0, and Child-Pugh class A or B.[1,2] According to this staging system, the optimal treatment for patients with early hepatocellular carcinoma (HCC) is liver transplantation (LT) because it involves the largest possible hepatectomy and removal of underlying cirrhotic tissue, leading to a much lower recurrence rate. Unfortunately, LT is not offered to all patients with early HCC as a result of the organ shortage, and patients decline due to tumor progression while waiting for a donor organ. So hepatic resection (HR) should be considered as the first-line treatment option for patients with a solitary tumor and well-preserved liver function.[3] However, the first-line treatment for patients with multifocal tumors meeting the BCLC stage A (≤3 nodules ≤3 cm) still remains unclear.

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Abbreviations and Acronyms

AFP = alpha-fetoprotein
BCLC = Barcelona-Clinic Liver Cancer
HCC = hepatocellular carcinoma
HR = hepatic resection
LT = liver transplantation
OS = overall survival
PHT = portal hypertension
RFA = radiofrequency ablation
RFS = recurrence-free survival

Since the introduction of radiofrequency ablation (RFA) for hepatic cancer in 1993, this technique has gained more attention than other local ablative modalities including percutaneous ethanol injection, percutaneous acetic acid injection, and microwave ablation for the treatment of HCC because of its high level of effectiveness and minimal invasiveness.[4-6] Radiofrequency ablation is also recommended as a curative treatment for early stage HCC patients (ie, BCLC stage 0 to A) in the practice guidelines of Western and Eastern countries.[3,7] Currently, the question about whether RFA can compete with HR as a first-line treatment for patients with early HCC remains controversial. Two randomized controlled trials showed opposite results.[8,9] On the other hand, 1 randomized controlled trial and other studies reported similar results for both HR and RFA in treating patients with early HCC.[4,10-13] In addition, the majority of studies focused their analysis mainly on early HCC patients with a single tumor. There are very few studies, to the best of our knowledge, exclusively evaluating outcomes for another type of early HCC meeting the BCLC stage A, that is, patients with multifocal tumors ($\leq$3 nodules $\leq$3 cm), treated by HR and RFA.

To clarify this issue, we compared the short- and long-term outcomes of HR and RFA patients with multifocal tumors meeting BCLC stage A. To delineate the differential survival benefits of HR and RFA in these patients, we determined prognostic predictors and performed subgroup analysis.

METHODS

This study was approved by the West China Hospital Ethics Committee, and in accordance with the ethical guidelines of the Declaration of Helsinki.

Definitions and diagnostic criteria

Clinically relevant portal hypertension (PHT) is defined as the presence of esophageal varices and/or a platelet count of less than 100,000 per μL in association with splenomegaly.[14]

For patients undergoing HR, HCC diagnosis was confirmed by histopathologic examination of the surgical samples. For those undergoing RFA, HCC diagnosis was confirmed by needle biopsy or by 2 types of clinical imaging, together with a high serum level of AFP and the background of HBV infection. If diagnosis was based on imaging and AFP level was uncertain, a needle biopsy was performed.

Patients

Figure 1 shows inclusion and exclusion criteria for the cohort. A total of 2,767 patients with HCC (not including the patients with recurrent tumors) underwent HR and/or RFA from January 2008 to February 2013 in our center. Of these, 487 patients had multiple tumors meeting the BCLC stage A. Next, 21 patients who had underwent other anti-tumor therapies before surgery were excluded, and 54 were excluded because they underwent HR and RFA simultaneously. After excluding 28 patients who were lost to follow-up, 384 patients who underwent HR or RFA were finally enrolled in this study. They were divided into 2 groups according to surgical procedures: the HR group (n = 224), which consisted of patients who underwent HR using the conventional open approach, and the RFA group (n = 160), which consisted of those who underwent RFA using percutaneous (n = 81), laparoscopic (n = 19), and open methods (n = 60). They were monitored until August 2014 or their death, and their medical records were retrospectively reviewed.

Selection of therapeutic method

Indications for HR were the presence of appropriate residual liver volume evaluated by CT or MRI. If the patients did not meet these conditions or the tumor was unresectable because of its special location, RFA should have been carried out. However, almost all of the patients enrolled in this study satisfied the indications for both HR and RFA because of the limitations for multifocal tumors meeting BCLC stage A and the technologic advances in hepatic surgery. In this case, they were informed that both HR and RFA were the radical therapeutic methods for their disease, and then selected the final therapeutic method. Both techniques were described in our previous study.[9] Generally speaking, when all tumors have percutaneous puncture routes under normal conditions or artificial serothorax, the percutaneous RFA procedure is recommended; as long as 1 tumor is located near the subhepatic inferior vena cava or gastrointestinal tract, the laparoscopic approach is recommended; if RFA cannot