

Shall we take a second thought before applying radiofrequency ablation for resectable HCC ≤ 2 cm?

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Abstract: Hepatocellular carcinoma (HCC), a disease with poor survival rates unless recognized and treated early, ranks as the fifth most common cancer worldwide. Previous researches have led some authors to choose radiofrequency ablation (RFA) as the primary treatment even the tumor is resectable. Dr. Roayaie's study retrospectively analyzed the surgical outcome of HCC ≤ 2 cm. The results obtained in the studies indicate that anatomic resection may achieve better survival for patients with well-preserved liver function, and without liver cirrhosis. This research also revealed the presence of satellite lesions and microvascular invasion were evident in such early tumors, as the benefit of anatomic resection is unique and cannot be duplicated by ablation. Further RCTs with large sample sizes and long-term follow-up are still required to clarify which should be the best treatment of choice.

Keywords: Hepatocellular carcinoma (HCC); early stage; anatomic resection

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Over 85% primary liver cancers are hepatocellular carcinoma (HCC) in China, mainly related to hepatitis B virus infection and cirrhosis. With nationwide efforts, alpha fetal protein (AFP), ultrasound screening and computed tomography for suspected cases could detect the tumor at an early stage when effective therapies can be applied. Small solitary HCC less than 2 cm in diameter was referred as "early (stage A)" or "very early (stage 0)" stage in Barcelona Clinic Liver Cancer (BCLC) system (1). Accordingly, resection, transplantation or radiofrequency ablation (RFA) was considered as curative therapies for Stage 0-A HCC. As liver transplantation removes both tumor and ill liver, it obtains the theoretically best curative effect with a median survival of 90 months (2). Surgical resection or ablation is proposed as the first-line treatment when facing to the scarcity of transplantation graft.

In the past decades, locoregional therapies for HCC have remarkably improved long term outcomes. A specific scenario for ablation is the very early stage of HCC. Patients with small HCC ≤ 2 cm and well-preserved liver function (Child-Pugh A) could expect 50-75% survival

rate at 5 years after RFA (3), thus paralleling the outcome of partial hepatectomy (4,5). Since the length of hospital stay after RFA was 6.7-8.7 days less than an open approach surgery, the similar life-expectancy at a lower cost than resection made RFA the most cost-effective therapeutic strategy in the Western countries. Therefore, promising results led some authors to choose RFA as the primary treatment even the tumor is resectable (6).

In recent issue of *Hepatology*, Roayaie *et al.* (7) evaluated the outcome of anatomic resection for early HCC ≤ 2 cm in two western centers. Their retrospective analysis between 1990 and 2009 identified a cohort of 132 patients. The outcomes of anatomic resection (n=76) were compared with non-anatomic resection (n=56). The 5-year survival was similar, but disease free survival rates (40% *vs.* 20%) were higher in the anatomic resection group. Authors found that 1-year recurrence rate classified by microvascular invasion, cirrhosis, and satellite tumors were all higher in the non-anatomic resection group. In another opinion, patients with cirrhosis (HR, 2.46) or platelet $<150,000$ (HR, 2.37) were associated with a worse 5-year survival.

Authors observed an overall recurrence rate of 17% at 1-year and 68% for 5 years. This was not so surprising for small HCC. Actually, similar high incidence of postoperative recurrence has been declared in other studies, such as a 3-year recurrence rate of up to 60% (8), and 61-69% in 5 years (9,10). Microvascular invasion, satellite nodules, advanced pathological stage and high AFP levels have been identified to be associated with HCC recurrence (11). Indeed, vascular invasion and intrahepatic metastasis are among the risk factors that most strongly influence the postoperative prognosis (12). Patients with vascular invasion and satellite lesion can be diagnosed immediately after a liver resection, while there was a 2-month delay for diagnosing "radiofrequency failure" after RFA.

This research revealed the presence of satellite lesions (12%) and microvascular invasion (27%) was evident in such early tumors. Approximately, 28% patients with solitary HCC ≤ 3 cm observed microvascular invasion (13), while this incidence increased with tumor size and number of tumors. Adequate tumor-free margin during surgical excision for very early HCC was an independent prognostic factor affecting the patient survival (14). The authors emphasized that anatomic resection was associated with a 20% decrease in the recurrence rate from 80% down to 60% at 5 years. Therefore, therapies should consider the potential tumor infiltration, as anatomic resection could eradicate intrahepatic metastasis with removal of one or more entire Couinaud's segments, the benefit of anatomic resection is unique and cannot be duplicated by ablation.

Dr. Roayaie's study found a 1-year recurrence rate of 17%, 5-year of 60% for anatomic resection group. These numbers overwhelmed that of RFA conducted in HCC of similar size reported earlier [34% at 1 year and 80% at 5 years (15)]. Moreover, our study (16) agreed with Roayaie's conclusion for solitary HCC ≤ 3 cm, the 1-year, 5-year survival rate of the RES group in our study was 100% and 82.2%, better than that of RFA group (91.2% and 61.4%). Moreover, our observed early tumor-recurrence (<2 years) was significantly higher in the RFA group than the RES group (38.3% *vs.* 22.6%).

The underlying liver disease, not only tumor factors, has been closely associated with the long-term survival (17). Hepatic resection in patients with chronic liver disease has always been challenging because of the clinical complexity of managing these patients and the potential risks associated with postoperative complications (18). With the development of surgical technology, compensated liver function (Child-Pugh B) is no longer the absolute contraindication for

hepatectomy (19). Indocyanine green (ICG) evaluation was helpful in predicting the risk of liver failure after resection. However, few clinical trials have yet achieved result in comparing the oncological outcomes between anatomic resection and RFA for HCC ≤ 2 cm in Child-Pugh B-C patients. Yamashita *et al.* reported that anatomic segmentectomy was no better than non-anatomic resection in Child-Pugh B patients with HCC ≤ 5 cm (20). More randomized trials are needed to optimize therapy for this scenario.

Dr. Roayaie's study retrospectively analyzed the surgical outcome of HCC ≤ 2 cm. The results obtained in the studies indicate that anatomic resection may achieve better survival for preserving liver function well, and without liver cirrhosis. However, further RCTs with large sample sizes and long-term follow-up are still required to clarify which should be the best treatment of choice.

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References

1. Bruix J, Sherman M; American Association for the Study of Liver Diseases. Management of hepatocellular carcinoma: an update. *Hepatology* 2011;53:1020-2.
2. Mazzaferro V, Regalia E, Doci R, et al. Liver transplantation for the treatment of small hepatocellular carcinomas in patients with cirrhosis. *N Engl J Med* 1996;334:693-9.
3. Germani G, Pleguezuelo M, Gurusamy K, et al. Clinical outcomes of radiofrequency ablation, percutaneous alcohol and acetic acid injection for hepatocellular carcinoma: a meta-analysis. *J Hepatol* 2010;52:380-8.
4. Lupo L, Panzera P, Giannelli G, et al. Single hepatocellular carcinoma ranging from 3 to 5 cm: radiofrequency ablation or resection? *HPB (Oxford)* 2007;9:429-34.
5. Chen MS, Li JQ, Zheng Y, et al. A prospective randomized trial comparing percutaneous local ablative therapy and partial hepatectomy for small hepatocellular carcinoma. *Ann Surg* 2006;243:321-8.
6. Lencioni R. Loco-regional treatment of hepatocellular carcinoma. *Hepatology* 2010;52:762-73.
7. Roayaie S, Obeidat K, Sposito C, et al. Resection of hepatocellular cancer ≤ 2 cm: results from two Western centers. *Hepatology* 2013;57:1426-35.
8. Fan ST, Ng IO, Poon RT, et al. Hepatectomy for

- hepatocellular carcinoma: the surgeon's role in long-term survival. *Arch Surg* 1999;134:1124-30.
9. Ueno S, Kubo F, Sakoda M, et al. Efficacy of anatomic resection vs nonanatomic resection for small nodular hepatocellular carcinoma based on gross classification. *J Hepatobiliary Pancreat Surg* 2008;15:493-500.
 10. Tanaka K, Shimada H, Matsumoto C, et al. Anatomic versus limited nonanatomic resection for solitary hepatocellular carcinoma. *Surgery* 2008;143:607-15.
 11. Tung-Ping Poon R, Fan ST, Wong J. Risk factors, prevention, and management of postoperative recurrence after resection of hepatocellular carcinoma. *Ann Surg* 2000;232:10-24.
 12. Izumi R, Shimizu K, Ii T, et al. Prognostic factors of hepatocellular carcinoma in patients undergoing hepatic resection. *Gastroenterology* 1994;106:720-7.
 13. Pawlik TM, Delman KA, Vauthey JN, et al. Tumor size predicts vascular invasion and histologic grade: Implications for selection of surgical treatment for hepatocellular carcinoma. *Liver Transpl* 2005;11:1086-92.
 14. Kim JM, Kang TW, Kwon CH, et al. Single hepatocellular carcinoma ≤ 3 cm in left lateral segment: liver resection or radiofrequency ablation? *World J Gastroenterol* 2014;20:4059-65.
 15. Livraghi T, Meloni F, Di Stasi M, et al. Sustained complete response and complications rates after radiofrequency ablation of very early hepatocellular carcinoma in cirrhosis: Is resection still the treatment of choice? *Hepatology* 2008;47:82-9.
 16. Huang J, Yan L, Cheng Z, et al. A randomized trial comparing radiofrequency ablation and surgical resection for HCC conforming to the Milan criteria. *Ann Surg* 2010;252:903-12.
 17. Bilimoria MM, Lauwers GY, Doherty DA, et al. Underlying liver disease, not tumor factors, predicts long-term survival after resection of hepatocellular carcinoma. *Arch Surg* 2001;136:528-35.
 18. Cucchetti A, Qiao GL, Cescon M, et al. Anatomic versus nonanatomic resection in cirrhotic patients with early hepatocellular carcinoma. *Surgery* 2014;155:512-21.
 19. Torzilli G, Belghiti J, Kokudo N, et al. A snapshot of the effective indications and results of surgery for hepatocellular carcinoma in tertiary referral centers: is it adherent to the EASL/AASLD recommendations?: an observational study of the HCC East-West study group. *Ann Surg* 2013;257:929-37.
 20. Yamashita Y, Taketomi A, Itoh S, et al. Longterm favorable results of limited hepatic resections for patients with hepatocellular carcinoma: 20 years of experience. *J Am Coll Surg* 2007;205:19-26.

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