



Radiofrequency ablation has similar short-term effects but significantly lowers the long-term effect compared with routine resection in the treatment of small hepatocellular carcinoma

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We read with great interest the recent article by Li and colleagues entitled “A systematic review and meta-analysis of radiofrequency ablation and routine resection in the treatment of small hepatocellular carcinoma” (1). The authors concluded that, compared with routine resection, radiofrequency ablation (RFA), which has lower complication rates and better clinical safety, can achieve similar short-term effects in the treatment of small hepatocellular carcinoma (SHCC) but has significantly lower 5-year effects. We quite agree with the authors about the effects and shortcomings of RFA, but have some comments on it.

Currently, hepatocellular carcinoma (HCC) is more frequently detected at an early stage in patients with regular surveillance, and appropriate treatment has become increasingly important. Among all therapeutic methods for HCC, liver transplantation and hepatectomy are the most effective and curative, especially for SHCC (2). Liver transplantation that meets the criteria can achieve the best prognosis, with the 5-year overall survival (OS) rate reaching 80% (3). However, several shortcomings, such as the higher surgical skills required, its high cost, and the shortage of donors, limit the widespread implementation of liver transplantation and thus, confine it to large medical centers (4). As a radical treatment, liver resection can achieve a similar effect to liver transplantation for SHCC patients at a lower cost and thus, has always been the first choice for SHCC, especially in young patients with good liver function (2).

RFA, as a local thermal ablation therapy, is being increasingly used in the treatment of liver cancer. However, a problem that clinicians must continually consider is how to provide individualized and optimal treatment plans for patients. As a minimally invasive treatment, RFA has better safety, especially in aged patients with poor performance status (5). A previous study (6) found that the 1- and 3-year OS rates of RFA had no statistical significance compared with liver resection. These results are comparable to those of Li and colleagues, with similar 1- and 3-year OS rates for RFA and conventional resection {odds ratio (OR): 0.78 [95% confidence interval (CI): 0.43–1.38], OR: 0.71 (95% CI: 0.48–1.05), and Z test: $P=0.32$ and $P=0.07$ (1)}. However, this is not to say that RFA could replace liver resection for the treatment of SHCC. Although small-sized studies have found that RFA of SHCC shows no difference in short-term OS compared with liver resection, long-term OS is still significantly lower than the latter. Liu *et al.* indicated that surgical resection had significantly better 5-year OS and recurrence-free survival (RFS) compared with RFA for single HCC ≤ 2 cm, with OS rates of 80% versus 66% ($P=0.034$) and RFS rates of 48% versus 18% ($P<0.001$), respectively (7). Li and colleagues reported the same results, in that the 5-year OS rate was significantly different between the RFA group and conventional resection group for SHCC [OR: 0.55 (95% CI: 0.40–0.72), Z test: $P<0.0001$] (1). The main reason for this is speculated to be related to the heat conduction principle of RFA ablation, whereby the heat is only conducted in a small area around the ablation needle,

and the heat effect is poor in the surrounding area (8). Although multiple puncture ablations can be performed, the heat conduction in the liver parenchyma after ablation is greatly reduced. Moreover, it is not easy to judge whether the ablation is successful during surgery because there are no definitive and quantifiable criteria. In addition, clinicians should strictly select patients who meet the indications for RFA (9).

RFA is not suitable for some locations because of the special thermal ablation effects, such as tumors in close proximity to large blood vessels and primary bile ducts. Blood flow in the large blood vessels can carry away some of the heat, which renders the energy surrounding the tumor insufficient to kill tumor cells. For tumors adjacent to the primary bile duct, low-energy ablation should be used to avoid bile duct stenosis and bile leakage caused by thermal damage, with the cost being not completely ablated to the focus. In addition, RFA could easily lead to the damage of adjacent organs, such as the stomach, duodenum, gallbladder, and heart, when ablating tumors on the edge of the liver. For tumors located in segments VIII and VII, RFA is difficult to perform because of the covering of ribs and the influence of the chest cavity and lung, which makes the needle puncture challenging. Therefore, the main indications of RFA include patients with tumors smaller than 5 cm, tumor location in the liver parenchyma, older age, and severe liver cirrhosis (5,9).

For multiple lesions, we could also choose to combine RFA with liver resection. Liver resection is performed for lesions on the liver edge adjacent to the major blood vessels and primary bile ducts, with RFA being performed for lesions located in the central liver parenchyma or those that are difficult to expose. Combining the two methods could maximize their respective advantages and achieve better therapeutic effects. To detect early recurrence, close postoperative follow-up is very important. Enhanced CT or MRI can determine whether there is an enhancement in the previous lesion and its surrounding area and whether tumor markers gradually decrease to normal levels. If residual or local recurrence is detected, liver resection, RFA, or other treatment methods can be reselected according to the actual situation of the patient. Repeat liver resection is associated with better long-term survival and local disease control in patients with a recurrent HCC ≥ 3 cm or alpha fetoprotein level ≥ 200 ng/mL (6,10).

Although RFA treatment of SHCC is associated with good short-term survival, fewer complications, and better safety, its long-term survival is still significantly lower than

that of liver resection. Therefore, liver resection is still the preferred treatment for young SHCC patients with good liver function and good tolerance to surgery.

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