

Percutaneous ablation for HCC eligible to transplantation: providing more opportunities of remission in the context of graft shortage

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Provenance: This is an invited Editorial commissioned by Editor-in-Chief Yilei Mao (Department of Liver Surgery, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Beijing, China).

Comment on: Lee MW, Raman SS, Asvadi NH, *et al.* Radiofrequency ablation of hepatocellular carcinoma as bridge therapy to liver transplantation: A 10-year intention-to-treat analysis. *Hepatology* 2017;65:1979-90.

Submitted May 07, 2018. Accepted for publication May 31, 2018.

doi: 10.21037/hbsn.2018.06.01

View this article at: <http://dx.doi.org/10.21037/hbsn.2018.06.01>

Liver transplantation (LT) is still considered as the best treatment for small HCC as compared to other curative therapeutic options such as resection and ablation, at least in theory. Recently Lee *et al.* (1) reported an excellent 10 years intention to treat overall survival in patients with HCC within Milan criteria after first line radiofrequency ablation followed by LT and challenged the alarming study of Llovet *et al.* about a risk of seeding in patients treated by percutaneous ablation before liver transplantation (2). For a long time, percutaneous monopolar radiofrequency ablation has been widely used to treat patients with small HCC not suitable for liver transplantation or liver resection (3). Despite the fact that percutaneous ablation has been included in the armamentarium of HCC curative treatments, most of the time patients treated by RFA in clinical practice are older, bear more comorbidities, portal hypertension or liver insufficiency as compared to patients eligible for liver resection (3). Such confounders explain the reported decreased survival and increased tumor recurrence in patients treated by RFA as compared to other modalities and consequently percutaneous RFA is still considered in several centers worldwide as a second-choice procedure

when other treatments are not feasible. However, several studies have suggested that monopolar RFA could obtain the same results in term of overall survival than liver resection in HCC of less than 2 cm developed on cirrhosis (4). Moreover, new ablation procedures such as multibipolar no touch RFA or irreversible electroporation allow to ablate difficult-to-treat lesions or increase the volume of ablation and the safety margin (5,6). As an example, multi-bipolar no touch RFA reaches up to 90% of complete necrosis at pathological reviewing as compared to 47% in monopolar RFA (6) and is associated with a better local control as compared to monopolar RFA in HCC of less than 3 cm (7). Overall, the place of RFA in the therapeutic algorithm of HCC developed on cirrhosis seems to be more complex than previously described. Frequently, patients with HCC on the waiting list are treated by TACE due to the theoretical risk of tumor seeding with RFA and the difficulty to perform liver resection in patients with cirrhosis with portal hypertension or impaired liver function. Finally, most of HCC treatments performed in patients awaiting transplantation encompass non-curative approaches such as TACE or more recently radioembolization with yttrium

90. Anti-tumoral procedures in patients with HCC awaiting transplantation are classically recommended if the waiting time exceeds 6 months. However, no randomized controlled trial support the potential benefit of such approach. Furthermore, there is no recommendation to favor one type of HCC treatment over another. Consequently, clinicians can only rely on retrospective data to guide routine practice. The study from Lee *et al.* reports the long term 10 years survival of patients with HCC treated by RFA as a bridge for liver transplantation (1). They show that “intention to treat” overall survival was 63.5% at 5 years and 41.2% at 10 years with post liver transplantation survival reaching 75.8% at 5 years and 42.2% at 10 years. The rate of drop out in the waiting list due to tumor progression was low (7.4%) and importantly tumor seeding was observed in only one patient in the setting of widespread metastasis. Percutaneous RFA was well tolerated (2.9% of major complications and no treatment related deaths). Finally, HCC recurrence post transplantation was only 5.6% (1). This important study underlines that RFA is a well-tolerated curative approach allowing remission in the waiting list of patients with HCC and is associated with good long term prognosis. Overall, clinicians have to face a competition between different therapeutic options in the waiting list. Liver resection is frequently not possible due to portal hypertension or liver function impairment and consequently TACE is widely used worldwide. However, as percutaneous RFA for HCC within Milan criteria is associated with better local tumor control and survival than TACE (8) and looking at the excellent results of the study of Lee *et al.*, percutaneous RFA should be considered as the most effective option in this setting in order to provide the best chances for curative management during the project of transplantation that per se is not always conducted to this end.

Moreover, organ shortage strongly limits the indication of liver transplantation as a first-line treatment in HCC patients. Consequently, sequential curative treatment using liver resection or RFA followed by liver transplantation as salvage has also been proposed with fair long-term results. We reported an intention-to-treat overall survival of 74% at 5 years, with only 31% of patients transplanted, leading to 69% of patients who were considered as “tumor-free” at the end of follow up suggesting that RFA could be also used as a first line treatment in transplantable patients with liver transplantation used only for salvage after tumor recurrence (9). Moreover, in the setting of graft shortage, this strategy appears to be cost-effective by avoiding LT

in patients with aggressive tumor (10). Overall, the role of percutaneous RFA in the therapeutic algorithm steadily increased in clinical practice and will continue to rise in the future with the development of new ablation procedures that aim to treat more efficiently the largest numbers of patients with HCC. Time has come to consider LT for patients with HCC within Milan criteria and without overt liver failure as a second line option if alternative conservative curative procedures such as percutaneous ablation have not provided long-term remission.

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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Cite this article as: Nault JC, Nahon P, Séror O. Percutaneous ablation for HCC eligible to transplantation: providing more opportunities of remission in the context of graft shortage. *HepatoBiliary Surg Nutr* 2018;7(4):302-304. doi: 10.21037/hbsn.2018.06.01