Editorial

Liver transplantation for the solitary intrahepatic cholangiocarcinoma less than 2 cm in diameter

Nobuhisa Akamatsu, Yoshihiro Sakamoto, Kiyoshi Hasegawa

Artificial Organ and Transplantation Surgery Division, Department of Surgery, University of Tokyo, Tokyo, Japan

Correspondence to: Nobuhisa Akamatsu. Artificial Organ and Transplantation Surgery Division, Department of Surgery, University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8655, Japan. Email: nakamats-tky@umin.ac.jp.

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The incidence of intrahepatic cholangiocarcinoma (ICC) has been increasing and is 1,000 times higher in hepatitis virus related cirrhotic livers than in non-cirrhotic livers (1,2). Following such background, liver transplantation (LT) had once been indicated for ICC, however, the dismal outcomes of LT for ICC in the early days has led ICC to be contraindicated for LT (3). On the contrary, the most recent researches on LT for ICC suggested that the outcomes of LT for "very early" ICC are comparable to those of hepatocellular carcinoma (HCC) (4). These backgrounds have resulted in the urgent necessity to investigate the impact of "very early" ICC, namely the incidental ICC with the diameter less than 2 cm, on LT recipients. Sapisochin and colleagues (5) performed the excellent large multicenter international retrospective study in a cohort of patients from 17 major LT centers worldwide, and confirmed that patients who were diagnosed with a very early incidental ICC at explant pathology after LT have an acceptable long-term survival and a low recurrence rate. The present results may have significant impact on the possible indication of LT for cirrhotic patients with a small solitary ICC.

Recently, we published a systematic review of LT for incidental/misdiagnosed ICC (6); the incidence of ICC was 0.34% (54/15,688), which was very similar to the present study (0.32%, 81/25,016). In this review, we found five articles investigating the outcome of LT for unrecognized ICC. Vallin *et al.* (7) found 10 incidental/misdiagnosed ICC cases (1%) among 993 LTs, in which the 1-, 3-, and 5-year actual survival rates were 80%, 60%, and 24%, respectively. Facciuto and colleagues (8) reported seven LT cases with preoperatively unrecognized ICC, in which the 5-year patient and recurrence free survival rates were 67% and 58%, respectively. Patkowski *et al.* (9) found 6 incidental ICC cases (0.5%) among 1,310 LTs, the outcome of which was dismal; the 1- and 3-year patient and recurrence-free survival rates were 75% and 25%, and 60% and 0%, respectively. Takahashi and colleagues (10) reported 13 incidental ICC cases (1%) out of 1,188 LTs. They reported that the 1- and 3-year recurrence-free survival rates were 67% and 42%, respectively. To note was that those with well-differentiated histology achieved the 3-year survival rate of 100%, while that of those with moderately-differentiated characteristics was only 22%. These are in accordance with the present study (5), indicating the poor differentiation as an independent predictor of impaired outcome of LT for very early ICC. Finally, Sapisochin *et al.* (11), in the Spanish multicenter study, reported 27 misdiagnosed ICC cases (0.34%) among 7,876 LTs, in which the 1-, 3-, and 5-year patient and recurrence-free survival rates were 78%, 66%, 51%, and 88%, 75%, 64%, respectively. In the same study, they firstly reported the excellent outcome of LT for those with cholangiocellular carcinoma characteristic tumors less than 2 cm. Based on the present multicenter large study (5) and the literature review, we are of the opinion that early ICC should not be considered as an absolute contraindication for LT.

One of the most important issues in discussing the indication of ICC for LT is the differential diagnosis from HCC. Indeed, 47% (7/15) were incidental, 53% (8/15) were misdiagnosed as HCC in the present study. In our literature review (6), 80% of the cases with preoperative identification of nodules were misdiagnosed as HCC preoperatively. Even with the recent advent of diagnostic modalities, we often encounter difficult nodules defining ICC, HCC or combined HCC/ICC only by radiologic findings (12). As the authors mentioned, tumor biopsy is necessary for a definitive preoperative diagnosis, however, it includes the risk of hemorrhage in cirrhotic patient and the tumoral seeding. In planning the prospective assessment or establishing a clinical guideline regarding the LT indication for ICC, the diagnostic criteria for ICC, especially very early ICC, should strictly be explained and agreed.

Another important issue is avoiding LT for those resection can be applied as a curative treatment. It is a matter of debate whether LT or resection should firstly be indicated for those both treatment options are applicable among patients with HCC (13). The same matter will take place among patients with early ICC. Looking at the first table of the present article (5), we assume that some of patients in “single tumor <2 cm” group could have undergone liver resection. The first treatment option for ICC patients who can tolerate liver resection both in terms of liver function and the tumor burden is definitely the resection (14). In addition, we recently reported that resection for solitary ICC less than 2 cm in diameter (very early ICC) could achieve a 5-year survival rate of 82.4% in a nationwide survey of the Liver Cancer Study Group of Japan (15). When restricted to very early ICC without portal invasion, a 5-year survival rate was 100% in the same study. Since the outcome of resection for ICC patients, if applicable, is equal to or even better than that of LT, the resectability should always be pursued in every ICC patient.

In conclusion, based on the present results and the previous literatures, cirrhotic patients with a solitary ICC less than 2 cm could undergo LT regardless of the preoperative definitive diagnosis of cholangiocellular carcinoma. Yet, clinicians should always be aware of the resectability of the lesion, since the liver resection can achieve equal or even superior patient survival for patients with very early ICC when compared to LT.

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Footnote

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

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