Editorial

# Ablative therapies for intrahepatic cholangiocarcinoma

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Among the 3 sub-types of cholangiocarcinoma (CH), [intrahepatic CH, hylar (CH) and extrahepatic (CH)], intrahepatic cholangiocarcinoma (ICC) accounts for up 8–10% of cholangiocarcinomas and 10–20% of all primary liver tumors (1). Interestingly, the occurrence of ICC on cirrhosis is increasing in the last years (2). Diagnosis of ICC mainly relies on histologic findings obtained with imaging guided biopsy when a hepatic lesion, usually single (small or large), is occasionally discovered in a healthy liver or in a cirrhotic liver during surveillance for hepatocellular carcinoma (HCC). At imaging, the suspicion of ICC is based on the findings of a hypovascular lesion or a hepatic nodule with a hypervascular rim on dynamic CT and/or MRI. On contrast enhanced ultrasound (CEUS), that usually is the imaging tool that should be immediately performed after the recognition of a liver lesion on conventional US, the dynamic contrast pattern is the same. Concerns may arise in patients with cirrhosis and the appearance of a small (<3 cm), single nodule with arterial enhancement mimicking HCC. The differential diagnosis is based on the very rapid wash out that is present in the ICC lesions, while the wash out of HCC appears in the very late phase, when present (3).

Due to the oncological aggressiveness of ICC respect to HCC, the treatment of choice of ICC is based on surgical resection that is the only cure that allows an increased survival (4).

Nevertheless, in recent years, with the increasing popularity of thermal ablation techniques in the treatment of HCC in cirrhosis, some researchers treated patients with ICC not eligible for surgery, with thermal ablation, on the basis of successful results of percutaneous treatment of HCC in cirrhosis (5-9,10).

In Vol 6, No 1 of February 2017 of *HepatoBiliary Surgery and Nutrition*, Shindoh performed a review on ablative therapies for ICC (10). Shindoh reported an analysis of the published series dealing with the results in treating ICC with ablative therapies mainly based on thermal ablation techniques (10). Patients with ICC undergoing thermal ablation are obviously not eligible for surgery or have had ICC recurrences after previous resection. Usually such patients are treated percutaneously and under ultrasound guidance. In the analysis of Shindoh radiofrequency ablation (RFA) was the most used technique, while microwaves (MWS) ablation was used only in a very few patients and with low powerful generators (10).

On the basis of published data, there are some considerations that can be made. Firstly, everyone obviously agrees that, up to now, all published studies include small number of patients and the number of studies is still too low. Moreover, the published studies include patients with a wide range in diameter of the nodules. Nevertheless, the data available so far show that RF thermal ablation of ICC nodules is feasible, easy to perform and effective, achieving appreciable volume of necrosis as is the case with the HCC (10). In fact, a technical effectiveness of 80–100% has been reported (10). The complication rates are negligible even in case of large nodules, and no death was reported (10). The second consideration is that the main ablation technique used so far by authors is RFA, and this explains

why the results of all published series indicate that only small nodules (<3–3.5 cm) can achieve a sufficient volume of necrosis compared with larger nodules. In these latter cases more ablation sessions (9) or cluster devices are required (10). In fact, to obtain a local tumor control at least similar to surgical resection, inducing a sufficient ablative margin of at least 0.5 to 1.0 cm surrounding the nodule is needed. With current technology, RFA is not the ideal tool to obtain similar results. In fact, thermal ablation induced by RFA has some disadvantages: its necrotic effect clearly decreases with the increase of tissue impedance and also when the tumors are located near to large vessels (11). Furthermore, using radiofrequency tumor ablation, volume decreases with the increasing of the diameter of the nodules, especially in tumors larger than 3 cm (12).

The third consideration is that the availability of the new high-powered microwaves today allows overcoming these disadvantages. MWS ablation has low sensitivity to local variation in tissue physical properties, such as impedance, and a lower susceptibility to convective heat loss from hepatic blood flow tissues when a nodule is located near to a large vessel (13). Modern MWS ablation provides wider ablation areas and faster ablation times compared to RFA, with an increasing in the sphericity of the area of necrosis (13). The availability of new powerful generators up to 200 watt and antennas operating at 2,450 MHz, allow to achieve very large volumes of necrosis in few minutes. Moreover, a margin of 0.5–1 cm of necrotic tissue can be easily obtained beyond the tip of the antenna. Therefore, from an interventional point of view, it is conceivable that when a ≤3–3.5 cm nodule is ablated with MWS for 3–5 minutes, an ablated area of 4–6 cm in diameter is easily obtained [one minute of a single antenna insertion determines 3.6 cm of necrosis (Giorgio A, unpublished data)] allowing a sufficient necrotic margin and therefore a better local tumor control.

Recently, Zhang *et al.* treated 107 patients with 171 ICCs <5 cm with MWS ablation (14). One, 3 and 5 years OS rates were 93.5%, 39.6% and 7.9%, with a median of 28.0 months. The median PFS after MWS ablation was 8.9 months; PFS rates at 6, 12, 18 and 24 months were 67.4%, 41.5%, 18.2% and 8.7%. There were no procedure-associated deaths. Child-Pugh class A and less tumour number were identified as factors predictive of prolonged PFS (14).

Yang and coworkers retrospectively analyzed the safety and efficacy of US guided MWS ablation combined with simultaneous transarterial chemoembolization in the treatment of 26 patients with advanced intrahepatic ICC (15). The complete ablation rate was 92.3%. There were no major complications. Median progression-free survival and overall survival were 6.2 and 19.5 months, respectively. The 6-, 12-, and 24-month survival rates were 88.5%, 69.2%, and 61.5%, respectively (15).

These results, although obtained in a not controlled manner and certainly with a still not very high number of patients, indicate that MWS ablation of ICC ≤3–3.5 cm is more effective than RFA. Therefore MWS ablation should replace RFA in treating ICC not amenable for surgery.

We agree with Shindoh that "*although only limited evidence from a small number of studies has been reported because of the rarity of this tumor*, *ablation therapies (mainly RFA) could be a treatment of choice for selected cases of ICC*" (10). Nevertheless, most likely RFA should be replaced by MWS ablation which, as mentioned before, that is able to ensure a complete ablation of tumor nodules <3–3.5 cm, determining a sufficient ablative margin of the tumor just for the properties inherent in the technique. Maybe, in the near future, with the increasing of experiences using MWS ablation such technique could become an alternative to surgery in treating small ICC, as it has happened with early HCC in cirrhosis.

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## Footnote

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

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