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Radiofrequency ablation of hepatocellular carcinoma extended into the portal vein: Preliminary results

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KEYWORDS
Hepatocellular carcinoma;
Cirrhosis;
Portal vein;
Tumor thrombus.

Abstract *Introduction:* We report our preliminary results of radiofrequency (RF) ablation of hepatocellular carcinoma (HCC) and neoplastic portal thrombus (NPT) in cirrhotic patients.
Methods: Ten patients (7 males and 3 females; mean age 68 yrs) with 10 HCC nodules (37—49 mm) extended into the main portal vein (MPV) underwent RF ablation. Diagnosis of NPT was achieved by fine-needle biopsy. RF ablation was performed firstly on the NPT and then on the HCC. RF ablation was considered successful when complete necrosis of the HCC and complete recanalization of the MPV were achieved. HCC necrosis was evaluated using contrast-enhanced CT. Recanalization of the portal vessels (PV) was analyzed using Color Doppler (CD). RF ablation was performed under ultrasonographic (US) guidance using a perfused electrode needle.
Results: Complete necrosis of the HCC with complete recanalization of the PV was observed in 7 patients (success rate: 70%). In the remaining 3, necrosis of the HCC ranged from 70% to 95%, and recanalization of the PV was not complete. No major complications occurred. In 2 cases, mild ascites and increased aspartate aminotransferase/alanine aminotransferase (AST/ALT) values were observed. The follow-up ranged from 4 to 24 months; 1 and 2-year survival rates were 77% and 77%, respectively. At the last follow-up, the 7 successful patients were alive and the portal system was still patent. The 3 unsuccessful patients died within 5 months due to progressive disease.
Conclusion: RF ablation can destroy HCC and NPT achieving a high rate of efficacy and low rate of complications. However, to confirm these results a control group and a longer follow-up are required.

Sommario *Scopo:* In questo studio riportiamo i dati relativi all'ablazione percutanea con Radiofrequenza (RF) di HCC e trombosi neoplastica dei vasi portali.
Pazienti e metodi: Dieci pazienti (pz) cirrotici, 7 maschi e 3 femmine, età media 68 anni, con 10 noduli di HCC e trombosi neoplastica dei vasi portali sono stati sottoposti ad ablazione

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percutanea con RF del trombo neoplastico e dell'HCC. La RF veniva ritenuta efficace quando alla TC con mdc si osservava la necrosi completa dell'HCC e al Color Doppler si osservava la ricanalizzazione completa dei vasi portali.
Risultati: La necrosi completa dell'HCC e la ricanalizzazione completa dei vasi portali si osservava in 7 (70%) dei 10 pazienti. Nei rimanenti 3 (30%) la necrosi dell'HCC e la ricanalizzazione dei vasi portali non risultavano complete. Non si osservavano complicanze maggiori. Tutti i pazienti venivano dimessi il giorno dopo la procedura. Follow-up 4—24 mesi. Le percentuali di sopravvivenza sono dell'80% ad 1 anno e del 70% a 2 anni. I 3 pazienti nei quali la procedura non è stata completamente efficace sono deceduti entro 5 mesi dalla procedura per progressione della patologia neoplastica. Nei 7 pazienti nei quali la procedura è stata efficace il sistema portale è a tutt'oggi completamente ricanalizzato.
Conclusioni: Questi primi risultati evidenziano che la RF è in grado di determinare necrosi completa della trombosi neoplastica dei vasi portali associata ad HCC con elevata efficacia e bassa percentuale di complicanze. Tuttavia questi risultati necessitano di ulteriori conferme e di un più lungo follow-up.

Introduction

Worldwide, hepatocellular carcinoma (HCC) is one of the most common forms of cancer, and it arises mainly in a cirrhotic liver. The incidence is about 3—4% per year, but screening programs have now permitted the diagnosis to be made at an early stage, when the tumor is eligible for curative treatment [1]. However, invasion of the portal vessels (PV) is still found in 12.5—39.7% of patients with HCC [1].

An HCC nodule invading the PV is crucial, and the prognosis is generally poor if the disease remains untreated, and a survival time ranging from 2.7 to 4.0 months has been reported [2,3]. Trans-arterial-chemoembolization (TACE), chemotherapy with 5-Fluorouracil (5-FU) in addition to Interferon, hepatectomy with or without tumor thrombus removal have been applied; however no standard treatment exists [4]. To our knowledge, HCC extension into the PV has not previously been considered an indication for percutaneous radiofrequency (RF) ablation [5—7]. However, on the basis of our experience [8] with one-shot percutaneous ethanol injection (PEI) in the treatment of large HCCs extended into the right or left branch of the portal vein, we wanted to treat cases of HCC extended into the PV using RF ablation. We therefore offered 10 consecutive patients to be treated with RF ablation and percutaneous thrombectomy of the portal vein tumor thrombus (PVTT) as an alternative to the above-mentioned options.

In this study we report the preliminary results of RF ablation of HCC with PVTT in 10 cirrhotic patients to verify the feasibility of the procedure (primary end-point) and the complications and survival (secondary end-point).

Materials and methods

From January 2005 to January 2007, 10 patients with 10 HCC nodules associated by neoplastic invasion of the left or right branches of the PV and main portal vein (MPV) were included in this study (Fig. 1). Seven patients were males and 3 females (mean age 68 years; range 63—72 years). Ethical approval for this study was granted by the Medical Research Ethics Committee of our hospital, and informed consent was obtained from all patients.

The diameter of the HCC nodules ranged from 37 to 49 mm (median 42 mm). All patients had liver cirrhosis: 8 were HCV-related and 2 were HBV-related. Nine patients had Child A cirrhosis (3 patients: C-P A5, 6 C-P A6) and one patient had Child B cirrhosis (C-P B7). No patient had ascites or other clinical signs of portal hypertension before RF ablation. Table 1 shows the characteristics of the patients of our series. Seven patients had HCC nodules located in the right lobe of the liver and 3 patients had HCC nodules in the left lobe. None of the nodules were in subcapsular location. In all 10 patients, international normalized ratio (INR) and platelet count ranged from 0.9 to 1.2 and 110 000 to 140 000, respectively. The right portal vein (RPV) branch was partially involved in 7 patients and the left portal vein (LPV) branch in the remaining 3. The MPV was involved in all cases: the length of PVTT ranged from 1.7 to 3.5 cm from the bifurcation and it was complete in all cases. Diagnosis of HCC was based on αFP, US

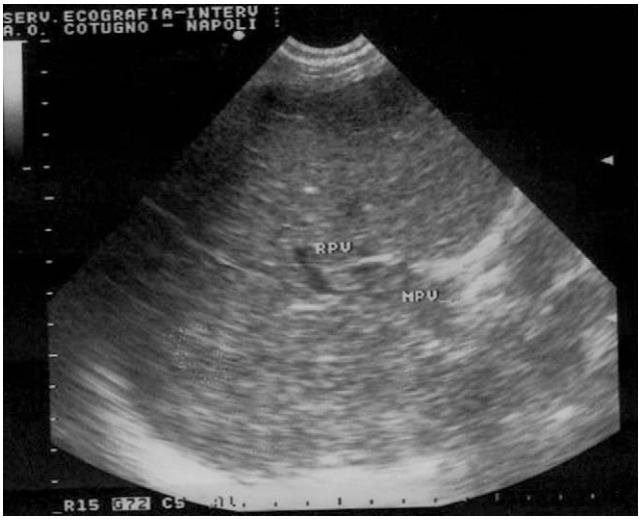

Fig. 1 Neoplastic thrombus in the main portal vein (MPV) and in the right portal vein (RPV).

Table 1 Baseline characteristics of the patients.

Patients	Child-Pugh class	HCC segment	diameter (cm)	Portal branch involvement	MPVTT length (cm)	MPV diameter (cm)
1	A5	II-III	3.8	Left	1.7	1.7
2	A6	II-III	4.1	Left	1.9	1.9
3	A6	II-III	3.9	Left	1.9	1.7
4	A5	VIII	4.1	Right	2.2	1.8
5	A6	IV	4.2	Right	2.7	2.0
6	A5	IV	4.0	Right	2.3	1.9
7	A6	V	4.4	Right	2.1	2.0
8	A6	IV	3.9	Right	2.8	1.8
9	B7	I—VIII	4.7	Right	3.5	1.9
10	A6	V—VI	4.9	Right	3	2

examination, contrast-enhanced ultrasound (CEUS), CT and/or MRI findings. Characterization of the HCC was made on the basis of early enhancement during the arterial phase and rapid wash out during the portal phase observed at CEUS, CT and/or MRI using contrast enhancement [9—11]. In all cases, HCC tumor thrombus was diagnosed by means of US guided fine-needle biopsy (21G needle; HS, Tokyo, Japan). RF ablation was performed under general anesthesia using a 1.7 or 2.0 mm perfused electrode needle (Integra HITT, Tuttingen, Germany) as reported in the literature [12].

Patients with HCC nodules located in the right lobe were treated while lying on their left side. The electrode needle was inserted percutaneously into the nodule and the right branch of the PV through the intercostal route. Patients with HCC nodules in the left lobe and tumor thrombus in the LPV branch were treated in supine position. In all cases, RF ablation of a tumor thrombus in the MPV was performed through the intercostal route with the patient lying on the left side. Figs. 2, 3 illustrate the RF ablation procedure on PVTT. RF ablation was performed firstly on the tumor thrombus in the main portal vein, then on the thrombus of the right/left portal branch, and finally on the HCC intraparenchymal nodule. The electrode needle was inserted percutaneously and the needle tip was advanced up to the posterior wall of the MPV. Care was taken to avoid the hepatic artery and common bile duct during the percutaneous insertion of the electrode needle into the MPV. Color Doppler (CD) helped to identify the hepatic artery. When the extension of the thrombus in the MPV exceeded 2 cm, two electrode needle insertions into the thrombus were performed without withdrawing the needle from the liver. The time employed for every insertion of the electrode needle ranged from 10 to 15 min and the time employed for the entire procedure (i.e. main portal vein, right or left branch vein and the HCC nodule) ranged from 25 to 45 min. At the end of the procedure, the portal vessels appeared hyperechoic. The procedure was considered successful when complete recanalization of the MPV, RPV or LPV and complete necrosis of the HCC nodules were achieved. Recanalization of MPV and portal branches was evaluated using CD and CEUS examinations; necrosis of the HCC nodules was evaluated using CEUS and contrast-enhanced CT. The day after RF ablation and once a week during the following 4 weeks, all patients underwent clinical and laboratory examinations, abdominal US, CD examination

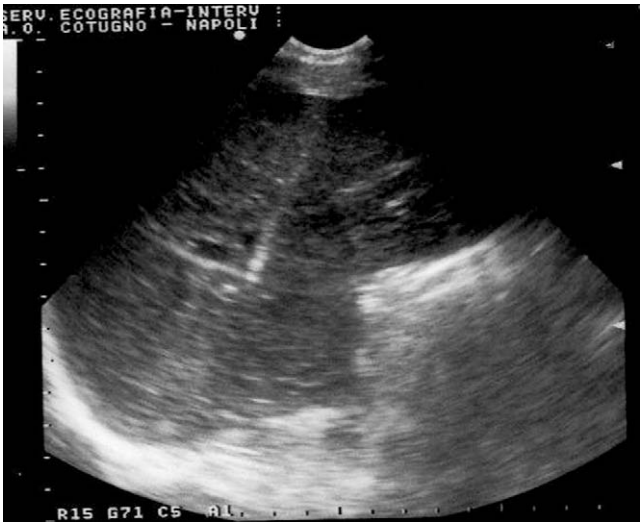

Fig. 2 The perfused needle electrode is percutaneously inserted into the tumor thrombus: the needle tip is inserted up to the posterior wall of the portal vein.

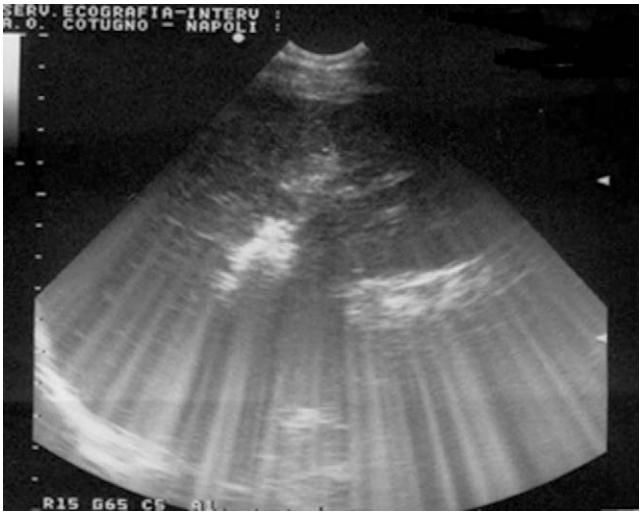

Fig. 3 After RF ablation the portal vein appears hyperechoic.

and CEUS. Abdominal US, CD examination, contrast-enhanced CT and CEUS were performed 1 month after the procedure. Contrast-enhanced CT was performed in order to evaluate the degree of necrosis of the HCC nodules, and CEUS was performed in association with CD as a complementary examination to identify HCC necrosis and to evaluate the patency of the PV. Clinical and laboratory tests, including αFP, abdominal US and CD examination were scheduled for every two months. Contrast-enhanced CT and CEUS were scheduled for every six months after the procedure.

Survival curve was calculated using the Kaplan—Meyer method.

Ethical approval for this study was granted by the Medical Research Ethics Committee of our hospital, and informed consent was obtained from all patients.

Results

The mean number of RF ablation sessions was 2 (range 1—3). Complete necrosis of the HCC nodules and complete recanalization of the PV (RPV or LPV and MPV) were observed in seven out of ten patients (success rate: 70%). Complete recanalization of the PV was observed at CD examination the day after the procedure in 2 patients, after one week in 4 (Fig. 4) and after 1 month in the remaining patient. Complete necrosis of the HCC nodules was achieved with a single RF ablation session in 5 of 7 patients, and with 2 RF ablation sessions in the remaining 2 patients. In all 7 successful patients, recanalization of the PV was accompanied by complete necrosis of the tumor. In the 3 unsuccessful patients, contrast-enhanced CT showed partial necrosis of the HCC (70—90%) and incomplete recanalization of the PV (in 2 patients: 90% necrosis on CT and unmodified PVTT on US and CD examinations; in 1 patient: 70% HCC necrosis and reduced length of the PVTT (from 2 cm to 1 cm)) at the bifurcation of the MPV.

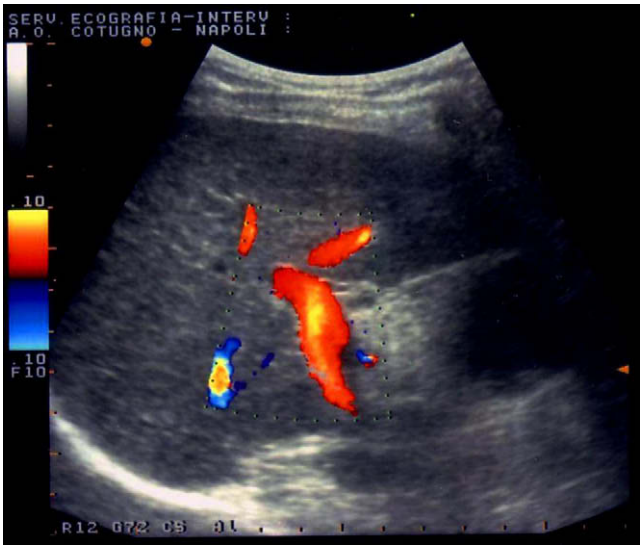

Fig. 4 One week later, CD examination shows complete recanalization of the MPV.

After the RF procedure, no major complications were observed; only 2 patients showed mild ascites and increased AST/ALT levels. Spironolactone was administered and the ascites disappeared within 1 week while AST/ALT returned to pre-treatment levels within 2 weeks. All patients were discharged from the hospital the day after the procedure. After RF ablation, diameter of the MPV ranged from 14 to 16 mm.

Follow-up ranged from 6 to 24 months. At the last follow-up, the 7 successful patients were all alive and the portal system was still patent in all of them; 1 and 2 year survival rates were 77% and 77%, respectively. Only 1 patient developed a distant hepatic recurrence 7 months after the procedure. The lesion was retreated with another session of RF ablation, and 1-month later complete necrosis was observed on contrast-enhanced CT and CEUS. The 3 unsuccessful patients died within 5 months of the procedure: 2 of them developed infiltrative neoplastic disease in the right lobe and 1 developed multiple HCC nodules.

Discussion

Worldwide, HCC is one of the most common forms of cancer, and it causes about 250.000 deaths per year [13]. The tumor arises mainly in a cirrhotic liver, and recent advances in imaging techniques (such as high defined US, enhanced CT and MRI) can detect it at an early stage. However, PV invasion is still found in 12—39% of cases and, not rarely, HCC extended into the PV is revealed only at the first diagnostic imaging examination. Many therapeutic modalities, such as liver transplantation, liver resection, PEI and RF ablation, have improved survival, but prognosis is very poor when the HCC has involved the major branches or the MPV, thus dramatically decreasing the overall survival from 2.4 to 4.8 months [1]. Many therapeutic options have been reported in the literature to improve survival, such as combined therapy of 5-FU and Interferon or TACE plus liver resection [13—18]. However, so far no standard treatment modality exists [4].

Percutaneous ablation techniques such as PEI and RF ablation have gained great popularity in the treatment of a single HCC nodule up to 5 cm, or 3 nodules up to 3 cm each, as complete response and improved survival can be achieved in selected patients [19,20]. However, PEI and RF ablation are usually not indicated in advanced cases of HCC [5—7].

In 1990 Livraghi et al. reported their first experience in the treatment of PVTT using PEI [21]. In 2000 we reported the results obtained in the treatment of large HCCs invading the right or left branch of the PV using one-shot PEI in 23 cirrhotic patients [8]. To our knowledge no study has so far been published on the use of RF ablation in a PVTT. Therefore, on the basis of the above-mentioned PEI experience, and in line with surgical removal of PVTT [14—18], we wondered if it would be possible to destroy the thrombus located in the portal vessels and over the intraparenchymal nodule using heat.

This preliminary experience seems to show that a percutaneous approach is feasible. In fact, 7 out of 10 treated patients showed complete recanalization of the MPV, RPV or LPV and complete necrosis of the HCC nodule.

Moreover, 1 and 2-year survival rates were 77% and 77%, respectively.

Chen and colleagues [14] surgically treated 438 patients with HCC and PV invasion: 286 of them had PVTT not extended into the MPV and were treated with hepatic resection only, while 152 patients had PVTT extended into the PV and were treated with hepatic resection and thrombectomy. Six months recurrence rates were 11.3% in the first group and 76.9% in the second group. The authors therefore concluded that liver resection with thrombectomy yields a better outcome in HCC patients with PVTT confined in the first or second branch of the PV compared to PVTT extending into the MPV.

Konischi et al. [15] reported the overall survival of 18 HCC patients treated with direct removal of the PVTT in the MPV. In their study the 1 and 2-year survival rates were 48% and 38%, respectively. Six patients who underwent complete removal showed 1 and 2-year survival rates of 75% and 75%, respectively. In 3 out of 5 patients who died within 90 post-operative days, incomplete removal of the PVTT caused early recurrence and death.

Our results seem to be similar to those obtained using a surgical approach, even though comparison is inappropriate as the series are very different.

Our results could be explained by the fact that the heat spreads into the main portal trunk thanks to a ''tunnel effect'', so that the solid neoplastic thrombus ''crumbles'' under the flux pressure in the portal vein and is removed. The duration of this ''pulverizing process'' can probably vary according to the tumor type. This would explain why a thrombus treated with RF ablation can disappear in 24 h or in 1 month or even right after the treatment, not disappear completely or not disappear at all. Moreover, if RF ablation does not cause complete necrosis of the intraparenchymal tumor, it will probably not produce a complete effect on the thrombus either, and vice versa.

Local control of the HCC nodules and recanalization of PV persisted for all the period of the follow-up. Unsuccessfully treated patients have a poor prognosis, and all 3 patients died within 5 months because of the further extension of the neoplastic disease.

The overall complication rate was very low in this study in comparison with the extent and number of ablation procedures. Only two patients had mild ascites and an increase in serum levels of AST/ALT, which returned to pretreatment levels in a few days. No other major complications were observed and no effect on the biliary tract was observed.

It is evident that our study has several limits. The main limit is the absence of a control group with the same characteristics who did not receive treatment. Another limit is the reduced number of patients and the lack of comparison with other types of therapies. Although our preliminary results are encouraging, RF ablation can mainly be considered a palliative treatment option in cases of advanced disease, but it should be carried out only by experts in interventional ultrasound.

In conclusion, our preliminary results show that RF ablation can destroy HCC associated with portal invasion in cirrhotic patients with a high rate of efficacy and low complication rates. However, to confirm these results a control group and a longer follow-up are required.

Conflict of interest statement

The authors have no conflict of interest.

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