

ORIGINAL ARTICLES

Therapeutic radiological interventional procedures in hepatocellular carcinoma

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Background: To improve the survival rate of patients with hepatocellular carcinoma (HCC) in whom surgery is not possible, various methods have been developed employing angiographic and percutaneous techniques. We analyzed our experience with various percutaneous therapeutic interventional techniques done for HCC in our center. **Methods:** Sixty-one patients with inoperable HCC (mean age 48.9 [SD 13.8] y; 47 men) were treated between January 1997 and December 2000 by transcatheter arterial chemoembolization (TACE) alone (22), TACE with percutaneous alcohol injection (PEI) (20), transcatheter arterial embolization (TAE) with steel coils and gel foam for gastrointestinal bleed (7), percutaneous radiofrequency ablation (1), percutaneous preoperative right portal vein embolization (3) and percutaneous preoperative tumor embolization to reduce blood loss at surgery (8). **Results:** In 42 patients treated by TACE and PEI and TACE alone, tumor necrosis was scored; over 50% necrosis was seen only after six and nine months in both treatment groups. The survival rates after six and nine months and the median survival were similar in the two groups. Of 7 cases treated with TAE with steel coils and gel foam, the gastrointestinal bleeding stopped in four; in the other three, bleeding did not stop completely although less transfusion was required. In the patient treated by radiofrequency ablation, follow-up contrast-enhanced CT did not show enhancing tumor mass. We noted left lobe enlargement after percutaneous preoperative right portal vein embolization, prior to right hepatectomy. **Conclusion:** In patients with HCC not amenable to surgical intervention, a variety of percutaneous therapeutic interventional techniques may be used. [*Indian J Gastroenterol* 2002;21:96-98]

Key words: Liver cancer treatment

Treatment of choice for patients with hepatocellular carcinoma (HCC) is surgical resection or liver transplantation in carefully selected cases. In patients with HCC not amenable to surgery, a variety of percutaneous therapeutic interventional techniques have been investigated. We analyzed our experience with these techniques.

Methods

We analyzed data of 61 consecutive patients with inoperable HCC (mean age 48.9 [13.8] y; 47 men) who were referred between January 1997 and December 2000 for various percutaneous interventional procedures, viz., transcatheter arterial chemoembolization (TACE) alone (22), TACE with percutaneous alcohol injection (PEI) (20), transcatheter arterial embolization (TAE) with steel coils and gel foam for gastrointestinal bleed (7), percutaneous radiofrequency ablation (1), percutaneous preoperative portal vein embolization (3) and percutaneous preoperative tumor embolization to reduce blood loss at surgery (8). The diagnosis was suspected on the basis of clinical and imaging features and α -fetoprotein (AFP) levels, and confirmed by preoperative fine needle aspiration biopsy or postoperative histology.

The commonest presenting features were abdominal pain, weight loss, anorexia, hepatic mass and symptoms or signs due to liver cirrhosis. Gastrointestinal hemorrhage as a presenting problem, which required urgent management with TAE with steel coils and gel foam, was noted in seven patients. Two patients presented with hepatic vein outflow tract obstruction. In one patient, tumor in the right lobe of the liver was extending into the right hepatic vein, causing its obstruction. Another patient had diffuse HCC with membranous obstruction of the right hepatic vein, liver cirrhosis, polycythemia and raised serum AFP levels; this patient presented with ascites and seizures secondary to hypoglycemia, suggestive of a paraneoplastic syndrome. We dilated the right hepatic vein through the right transjugular route along with other interventional treatment in these patients.

We treated 20 patients by TACE followed by PEI using multiple sessions and 22 patients with multiple sessions of TACE alone (Fig 1). Tumor (extent and number of lesions) was assessed using dual-phase helical computed tomography (CT). The inclusion criteria were: well-defined tumor larger than 10 cm in diameter, single or in association with few small daughter nodules with a maximum diameter of one centimeter, with no evidence of main portal vein thrombosis, arterio-portal or arterio-venous shunting, extrahepatic metastases, ascites or bleeding disorder. The primary tumors were encapsulated and

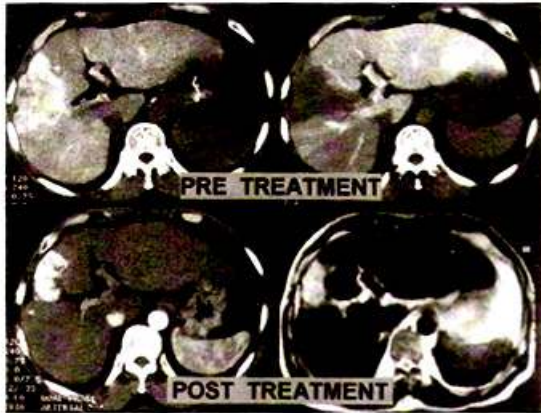


Fig 1: Pre-treatment dual-phase computed tomogram of liver showing vascular mass in segments IV and V, with reduction in size of mass after TACE

measured 116-144 mm (mean 128.2 SD [8.6] mm) in the greatest dimension in patients treated with TACE and PEI, and 114-148 mm (127.1 [8.5] mm) in patients treated with TACE alone. The chemotherapeutic agent used in both the groups was doxorubicin hydrochloride, 60 mg/m² body surface area, mixed with 8-10 mL of iodized oil (*Lipiodol Ultrafluid*; Laboratories Guerbet, Aulnay-sous-Bois, France) followed by gel-foam embolization after advancing a catheter into segmental or subsegmental arteries feeding the tumor. Response was assessed using serum AFP levels, and imaging techniques (ultrasonography, color Doppler, or contrast-enhanced helical CT). Tumor necrosis was scored in three stages (more than 50%, 50% or less, and absent or insignificant).

Seven patients who presented with massive, intermittent gastrointestinal bleeding were treated with TAE with steel coils and gel foam. The causes of gastrointes-

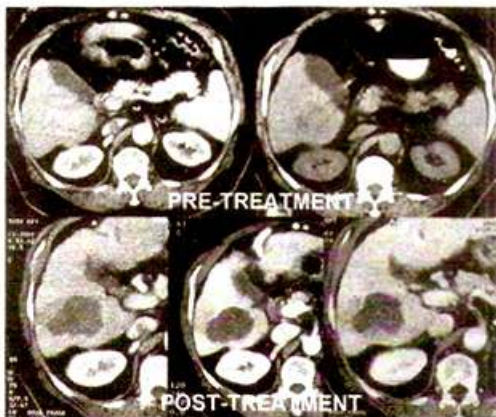


Fig 2: Pre-treatment computed tomogram of liver showing vascular mass (arrows) in segment VI, and complete necrosis and reduction in size (arrows) one year after radiofrequency ablation

tinal bleeding were varices secondary to tumor arterio-portal shunts (3), and direct invasion of duodenum (1), transverse colon (2) or stomach (1). We treated one patient with a 4 cm x 4 cm HCC in segment VI of a cirrhotic liver using single session of radiofrequency ablation using cooled-tip needle. Percutaneous preoperative right portal vein embolization was done in three cases with large HCC in the right lobe of the liver.

Results

In 42 patients treated by TACE and PEI or TACE alone, there was no significant reduction in size of the tumor, although AFP values remained variable in patients where no growth of mass was seen in the primary tumors. More than 50% necrosis on radiologic evaluation was seen only after six and nine months in both treatment groups. Survival rates after six (16/20 versus 16/22) and nine months (14/20 versus 13/22), and the median survival (7 months) were similar in the two treatment groups. Adverse effects included transient elevation of liver enzymes and fever in all patients. There was no treatment-related death.

Of 7 patients treated with TAE with steel coils and gel foam, gastrointestinal bleeding ceased in four. In three patients, bleeding did not stop completely although transfusion requirement decreased. The patient treated with radiofrequency ablation became symptom-free and follow-up dual-phase helical CT one year later showed no enhancing tumor (Fig 2). We noted left lobe enlargement on CT after percutaneous right portal vein embolization (Fig 3).

Eleven of 61 treated patients (TACE alone – 1, TACE with PEI – 1, TAE with steel coils and gel foam – 2, radiofrequency ablation – 1, percutaneous portal vein embolization followed by right lobe hepatectomy – 2 and preoperative tumor embolization – 4) were alive at

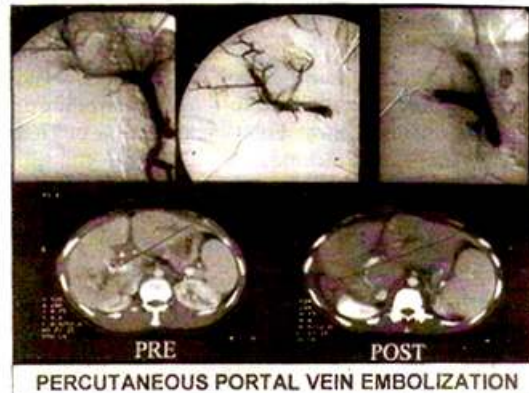


Fig 3: Right portal vein embolization with multiple steel coils (A, B) after percutaneous puncture under ultrasound guidance. Pre (C) and one week post (B) embolization computed tomogram show enlargement of left lobe of liver

one-year follow-up. The cause of death in the remaining patients was related to the malignancy.

Discussion

Surgical resection should be considered as the treatment of choice for patients with HCC. It is useful mainly for small (<5 cm), peripherally located tumors associated with good hepatic function; in such patients, it has a 5-year survival rate of 50%.¹ Causes of death in patients with HCC following surgical management show that the incidence of hepatic failure is high in postoperative patients;² postoperative hepatic failure can be prevented by pre-operative right portal vein embolization in patients with non-cirrhotic liver. After this procedure, there is redistribution of portal blood flow with hypertrophy of an initially inadequate future remnant liver (i.e., the segment of liver which is hypertrophied after this procedure and is the patient's future functional remnant liver).² We started doing this procedure under ultrasound and fluoroscopy guidance and now prefer to do it under ultrasound guidance alone.

PEI results in coagulative necrosis and fibrosis of the tumor. It is not indicated in patients who are candidates for liver transplantation or surgical resection. This technique is particularly useful for small lesions (<3 cm in diameter) but is not for larger lesions³ because residual neoplastic tissue can persist along the periphery of the nodule or in portions isolated by septae. It is contraindicated in lesions located close to the liver surface, and patients with ascites or coagulopathy. PEI can be done either alone or in combination with other therapeutic techniques like TACE or radiofrequency ablation. It is a simple, safe and cost-effective technique for small lesions.³

TACE alone or with PEI has better tumor response rate than with systemic chemotherapy. The commonly used chemotherapeutic agents are epirubicin, mitomycin-C and cisplatin.⁴

Transcatheter arterial embolization of tumor as an emergency procedure is done to reduce gastrointestinal hemorrhage. This is an unusual complication of HCC.⁵ We have found this technique useful in the control of bleeding; the angiographic technique and results of five of seven patients in this study have been reported earlier.⁶

Radiofrequency hyperthermia using the newly developed 'cooled-tip' needle is one of the latest ultrasound-guided percutaneous treatment techniques for HCC. Continuous cooling of the needle tip allows tissue heat-

ing and necrosis far from the electrode without tissue charring. Further experience is needed to better define the role of percutaneous thermoablation in the treatment of large HCC. In large tumors, it can be combined with PEI or TACE.⁷ Presently, this treatment is not widely available in India.

In conclusion, non-surgical treatment of HCC may slow tumor progression and provide palliation. Ablative percutaneous procedures, such as alcohol injection or radiofrequency thermal therapy, are most effective in the destruction of solitary tumors of 3 cm or less. Arterial embolization or chemoembolization has an anti-tumor effect but these should be avoided in patients with advanced cirrhosis.⁸

References

1. Lai EC, Ng Io, Ng MM, Lok As, Tam PC, Fan ST, et al. Long term results of resection for large hepatocellular carcinoma: a multivariate analysis of clinico-pathological features. *Hepatology* 1990;11:815-8.
2. Tanaka H, Hirohashi K, Kubo S, Shuto T, Higaki I, Kinoshita H. Preoperative portal vein embolisation improves prognosis after right hepatectomy for hepatocellular carcinoma in patients with impaired hepatic function. *Br J Surg* 2000;87:879-82.
3. Shiina S, Niwa Y. Percutaneous ethanol injection therapy in the treatment of liver neoplasm. In: Howard E, Ed. Current Techniques in Interventional Radiology. Philadelphia: Cope C. 1994;3:3.1-3.14.
4. Bartolozzi C, Lencioni R, Caramella D, Vignali C, Cioni R, Mazzeo S, et al. Treatment of large HCC: transcatheter arterial chemoembolization combined with percutaneous ethanol injection versus repeated transcatheter arterial chemoembolization. *Radiology* 1995;197:812-8.
5. Wettstein AR, Heuss LT, Meier R. Gastrointestinal haemorrhage in hepatocellular carcinoma. *Schweiz Med Wochenschr* 1998;128:1627.
6. Srivastava DN, Gandhi D, Julka PK, Tandon RK. Gastrointestinal hemorrhage in hepatocellular carcinoma: management with transhepatic arterioembolization. *Abd Imag* 2000;25:380-4.
7. Marone G, Francica G, D'Angelo V. Echo-guided radiofrequency percutaneous ablation of hepatocellular carcinoma in cirrhosis using a cooled tip. *Radiol Med (Torino)* 1998;95:624-9.
8. Llovet JM, Sala M, Bruix J. Nonsurgical treatment of hepatocellular carcinoma. *Liver Transpl* 2000;6 (6 Suppl 2):S11-S15.

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