Safety and Efficacy of Transarterial Chemoembolization in Patients with Unresectable Hepatocellular Carcinoma and Portal Vein Thrombosis

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PURPOSE: Despite the absence of conclusive data, portal vein (PV) thrombosis is considered a contraindication to transarterial chemoembolization (TACE) in patients with unresectable hepatocellular carcinoma (HCC). The purpose of our study was to establish the safety of TACE in such patients and identify key prognostic factors and survival.

MATERIALS AND METHODS: Data were prospectively collected from 32 consecutive patients with unresectable HCC and PV thrombosis who underwent treatment with TACE. History and physical examination, relevant laboratory values, and contrast material–enhanced magnetic resonance (MR) images were obtained before each TACE procedure. Repeated TACE was performed every 6 weeks unless patients developed a contraindication or MR imaging showed complete response.

RESULTS: Median overall survival was 9.5 months (range, 3–50 months). Child-Pugh numerical disease stage was the prognostic factor most strongly related to survival. The 30-day mortality rate was zero and there was no evidence of TACE-related hepatic infarction or acute liver failure. The 6-, 9-, 12-, and 18-month survival rates were 60%, 47%, 25%, and 12.5%, respectively.

CONCLUSIONS: PV thrombosis should not be considered a contraindication to TACE. Compared with historical control subjects who received traditional forms of treatment, the patients in the present study had extended survival. However, prospective randomized trials are necessary to show this conclusively and to show which subgroups benefit.

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Abbreviations: AFP = α-fetoprotein, HCC = hepatocellular carcinoma, TACE = transarterial chemoembolization, PV = portal vein

APPROXIMATELY 80%–85% of patients with hepatocellular carcinoma (HCC) have unresectable disease at presentation, leaving them with no curative option (1–3). The only options with curative intent are resection or transplantation, which are available to only 15%–20% of patients (1). Even then, recurrence rates of 20%–40% are observed (1). Despite its widespread use, it was only during the past 2 years that the efficacy of TACE was proven. Llovet et al (4) published results from a randomized controlled trial that was stopped early because TACE provided a statistically significant survival benefit in selected patients (survival rates at 1 and 2 years of 82% and 63% for TACE vs 63% and 27% for supportive care, respectively). A metaanalysis of five randomized controlled trials also concluded that TACE reduced 2-year mortality rates in patients with unresectable HCC (odds ratio, 0.54; 95% CI, 0.33–0.89; $P = .015$) (5). Additionally, Lo et al (6) showed statistically significant survival benefit in patients with unresectable HCC treated with chemoembolization with cisplatin and iodized oil. The 1-, 2-, and 3-year survival rates in TACE-treated patients were reported to be 57%, 31%, and 26%, compared with 32%, 11%, and 3%, respectively, in the control group. Finally, in a metaanalysis of randomized controlled trials, Llovet et al (7) showed significantly decreased 2-year mortality rates in patients treated with chemoembolization, with an odds ratio of 0.53 (95% CI, 0.32–0.89; $P = .017$).

A known complication of HCC is tumor or bland portal vein (PV) thrombus, which is considered by most to be an absolute contraindica-

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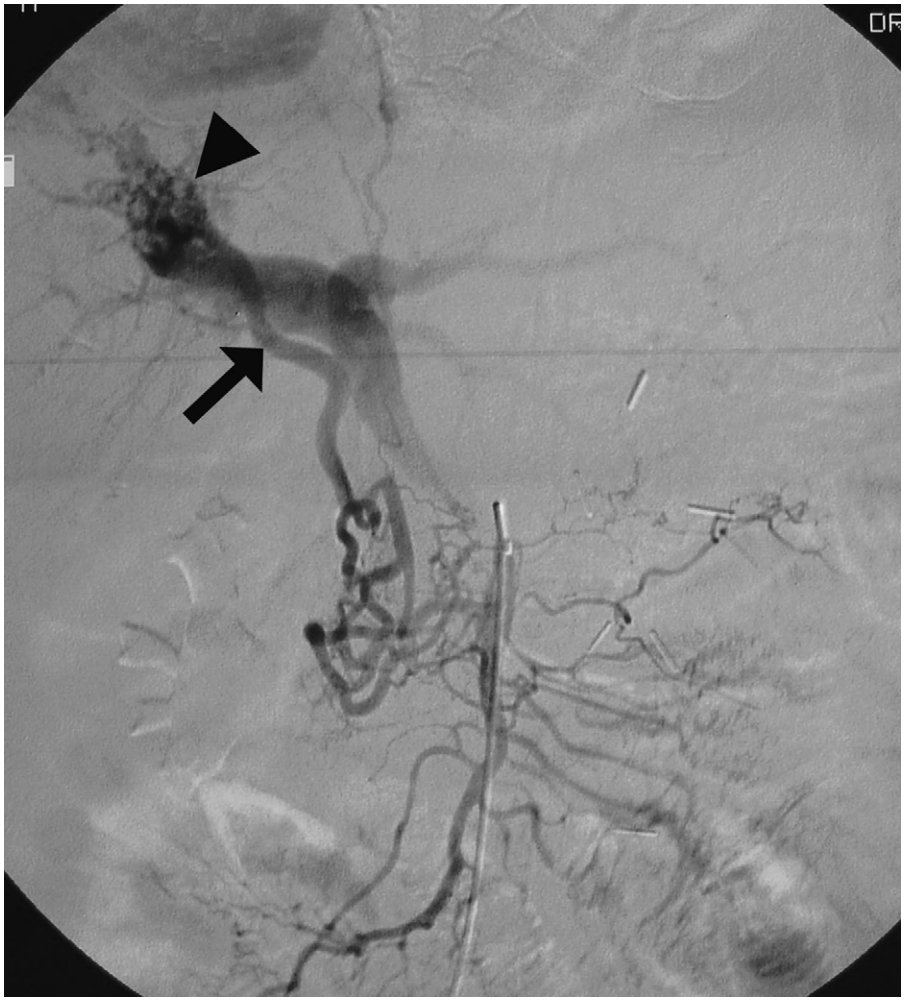

Figure 1. Superior mesenteric arteriogram shows the right hepatic artery (black arrow) supplying a vascular tumor (black arrowhead). The tumor (hepatocellular carcinoma) invades the right portal vein, which shows early contrast enhancement as a result of shunting. After gelfoam embolization, the shunt was eliminated and the tumor chemoembolized as per protocol.

tion to TACE or, at the very least, to represent an increased risk for complications after the procedure, including acute liver failure or infarction (5,6). It is well-established that patients with unresectable HCC and PV thrombosis have a worse prognosis than those without PV thrombosis irrespective of disease stage or treatment (8–11). As many as 38% of patients with unresectable HCC and 17% of those who are candidates for TACE have main, right, or left PV thrombosis (9). Autopsy series have revealed a much higher number, with nearly 70% of patients shown to have PV thrombosis if one includes isolated segmental branch thrombosis (11). Because of the high incidence of patients with unresectable HCC and PV thrombosis, it has become critical to study the safety and efficacy of TACE in such patients. The goals of our study were to determine whether TACE can be performed safely in patients with HCC and PV thrombosis and to correlate relevant variables with survival.

MATERIALS AND METHODS

Patient Group

From April 2000 to March 2004, data were collected prospectively in 32 consecutive patients with unresectable HCC and PV thrombosis who underwent one or more TACE procedures at our institution. This report was approved by the institutional review board as part of the approved TACE database. Patients had complete occlusion of the main PV, right PV, left PV, or both right and left PVs. The data analysis was performed in a retrospective fashion. Before intervention, patient management was discussed at a multidisciplinary liver tumor board, which included interventional and diagnostic radiologists, surgical and medical oncologists, and hepatologists, who reached consensus on the treatment plan. Fifteen patients had biopsy-proven HCC. The other 17 had hepatitis B–related, hepatitis C–related, or alcoholic liver cirrhosis with a hypervascular mass on computed tomography (CT) or magnetic resonance (MR) imaging and an α-fetoprotein (AFP) level greater than 400 ng/mL, factors considered diagnostic of HCC. Patients were seen in the clinic, history was recorded, physical examination was performed, and all relevant imaging and laboratory studies and clinical history were reviewed. PV thrombosis was diagnosed on dual-phase contrast material–enhanced CT and/or MR imaging and confirmed with angiography at the time of the first TACE procedure in all patients. Exclusion criteria for the 32 patients who underwent TACE (29 men and three women) included Child class C liver disease, uncorrectable bleeding diathesis, significant encephalopathy, or bilirubin levels greater than 3 mg/dL. Inclusion criteria were unresectable HCC, absence of extrahepatic disease, and Eastern Cooperative Oncology Group performance status of 0–3.

Technique

Chemoembolization technique.—All patients were premedicated with cefotetan 2 g intravenously (AstraZeneca, Wilmington, DE) before the procedure. In case of penicillin allergy, patients received clindamycin 600 mg intravenously (Pharmacia & Upjohn, Kalamazoo, MI). A superior mesenteric arteriogram with portal venous phase was initially performed to determine the extent of PV invasion or thrombosis (**Fig 1**) and show possible variant hepatic arterial supply. Then, the celiac axis was selected. Over a 0.035-inch Glidewire (Terumo, Somerset, NJ), a Simmons-1 catheter was advanced into the de-