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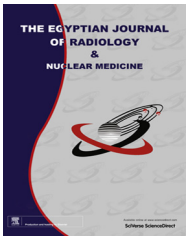

ORIGINAL ARTICLE

Radioembolization with Yttrium-90 resin microspheres in treatment of HCC with or without PVT: Initial Egyptian experience

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KEYWORDS

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Yttrium-90;
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Abstract *Background/Aim:* Hepatocellular carcinoma (HCC) is the most common primary malignancy of the liver. Radioembolization with yttrium-90 (Y-90) microspheres is a new concept in radiation therapy for HCC. The aim of this study is to evaluate efficacy, side effects, and future direction of Y-90 therapy, using TheraSphere®, in patients with HCC with or without PVT.
Patients and methods: Forty patients were presented by hepatocellular carcinoma most of them with portal vein thrombosis and were treated with Y-90 resin microspheres (SIR-TeX®).
Results: At one month after treatment the overall response (complete or partial response) was exhibited by 9% of patients, stable disease exhibited by 80% of patients, progressive disease seen in 11% of patients.
Conclusion: Radioembolization with Y-90 resin microspheres offers a favorable risk/benefit profile for patients presenting with locally advanced unresectable HCC with or without PVT and good liver function.

1. Introduction

Hepatocellular carcinoma (HCC) is the most common primary malignancy of the liver, it claims half a million lives across the globe each year (1). It is the sixth most common cancer in the world and is the third most common cause of cancer-related mortality (2). Resection and transplantation are the only curative treatments at present. However, the role of surgery is restricted. Resection can only be done in patients with normal liver function and transplantation is only possible in

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patients who satisfy the Milan criteria (3). The only systemic chemotherapeutic drug that has shown some potential in managing HCC is Sorafenib (4).

Standard therapy for patients with larger tumor sizes and no macrovascular invasion is transarterial chemoembolization (TACE).

TACE has been shown to prolong the survival in patients with BCLC (Barcelona clinic liver cancer) staging stage B (intermediate stage), (5) But has failed to show survival benefit in patients with advanced HCC, even in those patients with adequate hepatic functional reserve (6). Therefore, in the current adaptation of the BCLC treatment algorithm the therapy of choice for advanced HCC is systemic treatment with sorafenib (7). This multikinase inhibitor has recently been shown to prolong the survival in patients with advanced HCC in a randomized, controlled phase III trial, (8) and is the first drug ever approved for the treatment of HCC. Due to the adverse effect profile of sorafenib, many patients can only tolerate a reduced dose or must discontinue the medication. This fact causes an ongoing effort to develop a locoregional treatment approach to patients with advanced HCC that is effective, but with a more acceptable/favorable toxicity profile than systemic therapy. Radioembolization with yttrium-90 (Y-90) resin microspheres is an emerging treatment for unresectable liver disease in patients who are not amenable to liver transplantation, resection, or selective ablative techniques (e.g., radiofrequency ablation or percutaneous ethanol injection) (9,10). The microspheres loaded with Y-90 are delivered to liver tumors by means of endovascular catheters selectively placed within the hepatic arterial vasculature (11).

The therapeutic advantage of the hepatic arterial approach is based on the unique dual vascular supply of the liver. It is known that hepatic tumors receive 80%–100% of afferent blood exclusively from the hepatic artery. Radioembolization takes advantage of this to provide liver-directed transarterial therapy (12).

The microspheres lodge preferentially within the neovessels of the tumor(s) and deliver high-energy radiation over a limited range (mean penetration of radiation into tissues is 2.4 mm), thereby minimizing the radiation exposure to normal liver parenchyma (11). Radioembolization differs substantially from transarterial chemoembolization (TACE). In TACE, the occlusion of medium and large size arteries (with the use of particles 3–10 times larger than those used in radioembolization) results in tumor ischemia that drives an antitumor effect, with drug delivery potentially enhancing tumor cell killing (13).

Radioembolization has two distinct aspects of the procedure: the first being the injection of embolic particles (“embolization”) as the vehicle and the second being the delivery and administration, via this embolic vehicle, of radiation (“radio”).

Hence, in patients presenting with PVT, there is a concern of an increased risk of liver failure as a result of the preexistent reduction of portal flow and the incremental compromise of arterial hepatic perfusion caused by the embolization of microspheres in the hepatic micro- and macrovessels. As a result, Y-90 microsphere therapy has historically been contraindicated in patients presenting with PVT (14,15). Recent studies with Y-90 glass microspheres have suggested that the original safety concerns regarding the risk of hepatic compromise in patients presenting with PVT may have been unfounded (16). An intense embolizing effect of glass microspheres has been recently ruled out by analyzing the pattern of arterial blood flow after contrast agent power injection immediately after treatment (17).

2. Patients and methods

Forty patients with unresectable HCC were referred from Clinical Oncology Department to be treated by radioembolization using Y-90 resin microspheres (SIR-TeX) during a period of 12 months between August 2011 and August 2012 at Ain Shams specialized hospitals.

Inclusion criteria for treatment included (1) HCC by imaging or pathology (2) nonsurgical candidate; not fit for radiofrequency or TACE (3) noncompromised pulmonary function (assessed by the history of severe chronic obstructive pulmonary disease, physical examination, and auscultation); (4) able to undergo angiography and selective visceral catheterization; (5) Portal vein thrombosis has been regarded as a relative contraindication to such treatments as TACE; however, it is not necessarily a contraindication to radioembolization; (6) tumor less than 70% of the total liver volume (5) adequate hematology (granulocyte count $\geqslant 1.5 \times 10^9$/L, platelets $\geqslant 50 \times 10^9$/L), renal function (creatinine $\leqslant 2.0$ mg/dL); (6) liver function (bilirubin $\leqslant 2.0$ mg/dL).

Exclusion criteria were (1) other planned therapy systemic/locoregional therapy for their cancer; (2) liver failure (bilirubin > 2.0 mg/dL); (3) evidence of any uncorrectable flow to the gastrointestinal tract observed on angiography or technetium-99m macroaggregated albumin scan; (4) greater than 30 Gy (16.5 mCi) estimated to be delivered to the lungs in a single administration or 50 Gy on multiple administrations; and (5) significant extrahepatic disease. Of note, patients were not excluded from therapy on the basis of portal hypertension or hepatofugal flow.

2.1. Treatment protocol

- Patients underwent a planning angiographic study to identify vascular anatomy, HCC feeding vessels, aberrant vessels and extrahepatic collateral vessels feeding extrahepatic organs (especially the gastrointestinal tract), and the presence of intrahepatic or intratumoral arterioportal shunting.
- Aberrant hepatic vessels and extrahepatic collaterals were coil-embolized to prevent the inadvertent misplacement of Y-90 resin microspheres into the gastrointestinal tract or pancreas. Technetium Tc 99m–labeled MAA particles were then injected with the delivery catheter in the intended position for Y-90 resin microsphere infusion.
- The major approach for the delivery of microspheres was lobar infusion, although segmental application of microspheres had to be used occasionally to prevent visceral shunting. If a bilobar infusion of Y-90 microspheres was planned, this was performed sequentially and the time between both treatments was 3–4 weeks.
- All the patients underwent 99mTc-MAA planar imaging to assess pulmonary shunt and any unintended flow to other extra-hepatic organs. An elevated hepatopulmonary shunt leading to exposure of the lungs of > 30 Gy in a single