CLINICAL STUDY

Cost Effectiveness of Radioembolization Compared with Conventional Transarterial Chemoembolization for Treatment of Hepatocellular Carcinoma

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ABSTRACT

Purpose: To assess cost effectiveness of radioembolization versus conventional transarterial chemoembolization.

Materials and Methods: The cost of radioembolization versus conventional transarterial chemoembolization was determined based on Medicare reimbursements. Three patient subgroups were defined based on the Barcelona Clinic Liver Cancer (BCLC) classification system (A, B, or C). Efficacy and safety outcomes after each procedure were obtained from the literature. A Monte Carlo case-based simulation was designed for 60 months in 250 patients in each subgroup. Survival was calculated based on average survival from the literature and the Monte Carlo model. The primary outcome was the cost effectiveness of radioembolization over transarterial chemoembolization by considering calculated survival.

Results: The costs approached $17,000 for transarterial chemoembolization versus $31,000 or $48,000 for unilobar or bilobar radioembolization, respectively. Based on the simulation, median estimated survival was greater with transarterial chemoembolization than radioembolization in BCLC-A and BCLC-B subgroups (40 months vs 30 months and 23 months vs 16 months, respectively, $P = .001$). However, in the BCLC-C subgroup, survival was greater with radioembolization than transarterial chemoembolization (13 months vs 17 months, $P = .001$). The incremental cost-effectiveness ratio of radioembolization over transarterial chemoembolization in the BCLC-C subgroup was $360 per month. The results were dependent on bilobar versus unilobar radioembolization and the total number of radioembolization procedures.

Conclusions: The model suggests radioembolization costs may be justified for patients with BCLC-C disease, whereas radioembolization may not be cost effective in patients with BCLC-A disease; however, many patients with BCLC-C disease have extensive disease precluding locoregional therapies. Secondary considerations may determine treatment choice in more borderline patients (BCLC-B disease) because there is no persistent survival benefit with radioembolization.

ABBREVIATIONS

BCLC = Barcelona Clinic Liver Cancer, HCC = hepatocellular carcinoma, ^{90}Y = yttrium-90

Hepatocellular carcinoma (HCC) is the sixth most common cancer worldwide and ranks as the third most common cause of cancer-related mortality (1–4). The overall per-patient cost of HCC is estimated to be $32,907 per year (5). Considering an average annual HCC prevalence of 13,824 cases in the United States, the total annual cost of HCC was estimated to be $454.9 million in 2006 (5). As the incidence of HCC continues to increase in the United States (6–8), costs associated with its detection, treatment, and complications are also expected to increase.

The treatment of HCC has been difficult because of the late presentation of disease (7). However, survival trends have shown improvement (8) for at least two reasons. First, HCC is being diagnosed at earlier stages through use of screening techniques such as ultrasound (8,9). Second, a significant survival benefit has been gained with locoregional therapies (10,11). Radioembolization and conventional transarterial chemoembolization are two known locoregional therapies in practice. Although radioembolization with yttrium-90 (^{90}Y) has

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Tables E1–E4 are available online at www.jvir.org.

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been shown to be effective in down-staging of HCC (12,13), very few studies have shown overall survival benefit for patients treated with radioembolization compared with transarterial chemoembolization (14). Radioembolization is a more expensive treatment than transarterial chemoembolization. The costs from the implementation of radioembolization include expenses related to ^{90}Y spheres and the evaluation performed before the procedure, which includes mapping angiography, a technetium-99m macroaggregated albumin scan to evaluate for the presence of a hepatopulmonary shunt, and single photon emission computed tomography/computed tomography (CT) imaging studies. In contrast, the costs involved with transarterial chemoembolization are related to the procedure itself and the associated overnight hospitalization. Given the limited treatment options for patients with advanced disease, it becomes challenging to determine the best approach for patients, especially in an environment where health care dollars are limited.

The purpose of this study was to model a cost-effectiveness analysis comparing radioembolization with transarterial chemoembolization using a case-based design. We hypothesized that using radioembolization is not well justified by the current cost figures for all the different patient groups with HCC. We sought to compare the financial burden of radioembolization versus transarterial chemoembolization for the treatment of unresectable HCC in the United States based on Medicare reimbursement values and per unit of gained survival.

MATERIALS AND METHODS

Study Design

This study entailed a systematic review of the literature followed by modeling for cost-effectiveness analysis and was exempt from institutional review board approval. Because HCC imposes a complex pathophysiologic process, we employed three of the most commonly encountered clinical scenarios relevant to the use of these treatment modalities. Liver functional reserve is also a determining factor for the success of treatments for HCC, especially in the radioembolization procedure (4). The natural history of HCC usually varies by Child-Pugh classes with 1-year survival rates of 20.6% Child-Pugh A, 8.4% Child-Pugh B, and 6% for Child-Pugh C (15). We used the Barcelona Clinic Liver Cancer (BCLC) classification system (A, B, or C) for the extent of disease because this system takes into consideration Child-Pugh classification as the indicator of functional reserve of the liver (**Table E1** [available online at *www.jvir.org*]). Although guidelines recommend using locoregional therapies only for BCLC-B disease, transarterial chemoembolization and radioembolization are often used outside this single group of patients, and we used the published data on the outcomes after use of these two treatment modalities on BCLC stages A, B, and C.

Systematic Review of Literature

A literature review was performed to obtain the probabilities of different outcomes after transarterial chemoembolization or radioembolization for unresectable HCC. The search was performed using MEDLINE, Web of Science, and EMBASE. Conference proceedings were excluded because of lack of detailed outcomes reporting for patients with different stages of HCC. Only articles in English were included. The search was performed from 2003–2013 to include the most recent experience. Review articles, letters, and commentaries were excluded. Key words used were "hepatocellular carcinoma," "hepatic arterial embolization," "chemoembolization," "radioembolization," "transarterial chemoembolization," "conventional transarterial chemoembolization," "liver transplantation," "^{90}Y," "yttrium-90," "locoregional therapies," and all combinations. The search was extended further to all relevant references in the bibliography of retrieved articles as well as the "related articles" featured in PubMed. All original studies that involved intraarterial treatment of HCC in unresectable disease were included in our review. Exclusion criteria included studies that did not report clinical outcomes or involved only technical features, had < 10 patients, did not report clinical outcomes classified by BCLC stages of HCC, involved only intraarterial chemical ablation without embolization, combined the tyrosine kinase inhibitor sorafenib with radioembolization, included only patients with portal vein thrombosis, or included metastatic disease to liver.

Calculation of Outcomes by Monte Carlo Modeling

The probabilities of outcomes were collected from the literature for three predesigned subgroups of patients. The Monte Carlo model was employed for simulating HCC cases from the time of diagnosis until death or up to 5 years (60 mo) (16). For each treatment type, patient subgroup, and recurrence rate, 5,000 iterations of the simulation were conducted based on previous reports (17). We designed each subgroup with 250 patients (**Fig**) (18). The probability of outcomes in each month was calculated for each iteration. The outcome of a subsequent month was determined based on the current month with the total probability of possible events equaling to 1.

Study Assumptions and Sensitivity Analyses

We assumed patients would undergo repeat transarterial chemoembolization procedures every 10 months, and so the simulation time was broken into 10-month intervals.