Journal of Cancer Research and Practice 3 (2016) 34–38

Contents lists available at ScienceDirect

Journal of Cancer Research and Practice

journal homepage: http://www.journals.elsevier.com/journal-of-cancer-research-and-practice

Original article

Comparison of surgical resection and transarterial chemoembolization for patients with intermediate stage hepatocellular carcinoma

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ARTICLE INFO

Article history:
Received 14 October 2014
Accepted 26 March 2015
Available online 19 March 2016

Keywords:
Intermediate-stage hepatocellular carcinoma
Surgical resection
Transcatheter arterial chemoembolization
Alpha-fetoprotein
Cirrhosis

ABSTRACT

Objective: Current guidelines recommend transarterial chemoembolization (TACE) as the standard treatment for patients with intermediate stage hepatocellular carcinoma (HCC). However, choosing the optimal treatments for patients with intermediate stage HCC still remains challenging for clinicians. The purpose of our study was to compare the long-term survival of intermediate stage HCC patients treated with surgical resection or TACE.

Methods: We obtained the baseline characteristics of 210 intermediate stage HCC patients that were recruited for this study. Survival analysis was performed by Kaplan–Meier method and a comparison was made by log-rank test. Factors associated with survival rate were analyzed by Cox's regression.

Results: There were 164 men and 46 women in the study group, with a mean age of 63 ± 11 years (range, 31–92 years). Among them, 67 patients (31.9%) received surgical resection and 143 patients (68.1%) received TACE. Patients receiving surgical resection had a significantly larger mean of maximum tumor size (6.8 ± 2.8 vs. 5.8 ± 3.2 cm, $P = 0.016$), higher ratio of solitary tumor (68.7% vs. 17.5%, $P < 0.001$), and Child-Pugh class A (97% vs. 85%, $P = 0.009$) than those with TACE. Patients receiving surgical resection had a significantly higher 1, 3, and 5 year survival rate compared with those treated with TACE (87.4%, 62.8% and 57.3% vs. 58.1%, 29.9% and 16.6%, $P < 0.001$). Multivariate analysis revealed that AFP level >400 ng/ml [hazard ratio (HR):2.141, 95% CI: 1.091–4.203, $P = 0.027$], Child B cirrhosis (HR: 4.726, 95% CI: 1.021–21.884, $P = 0.047$), and TACE (HR:3.391, 95% CI: 1.625–7.076, $P = 0.001$) were independent risk factors associated with poor prognosis.

Conclusions: Our results indicated that surgical resection provided superior survival benefit than TACE to patients with intermediate-stage HCC. This is in part attributable to advances in liver surgery which make the resection of intermediate-stage HCC possible. Surgical resection should be considered first for patients with preserved liver function.

1. Introduction

Hepatocellular carcinoma (HCC) is one of the most common cancers in the world. More than 75% of HCC cases occur in the Far East and Southeast Asia.[1] Only a small proportion of patients have their HCC detected in an early curable stage, thus the worldwide 5-year survival rate of HCC only slightly increased from 5 to 15% over the past two decades.[2] The major causes of unsatisfactory prognosis of HCC include degree of liver function impairment and heterogeneous nature of HCC, which affect treatment outcome.[3] Cumulative evidence also suggests that accurate assessment and staging of HCC, and correct designation of optimal treatments may prolong survival rate of HCC.[4,5] Among current HCC staging systems, the Barcelona Clinic Liver Cancer (BCLC) classification is the one of most

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Peer review under responsibility of The Chinese Oncology Society.

http://dx.doi.org/10.1016/j.jcrpr.2015.03.001

reliable for prognosis prediction at the time of HCC diagnosis.[6,7] To be categorized as BCLC intermediate-stage, patients are asymptomatic (performance status score, 0) with multinodular tumors but without vascular invasion or extrahepatic spread. The median survival time was 16 months for patients with BCLC intermediate-stage HCC.[6] Based on the AASLD guideline, a revised version of the Barcelona Clinic Liver Cancer (BCLC) staging system by the American Association for the Study of Liver Diseases (AASLD),[4,5] transarterial chemoembolization (TACE) has been recognized as an effective option for those with intermediate stage HCC.[4,5,8] Although TACE has been considered a palliative treatment for unresectable HCC, previous meta-analyses indicated that treatment with TACE is associated with a significantly higher 2-year survival rate than those patients receiving conservative management or suboptimal therapies.[9,10] Nonetheless, the improvement in long-term survival is not clear. In addition, TACE-associated adverse events include post-embolization syndrome, relevant liver function deterioration, ascites and gastrointestinal bleeding; such adverse events are not unusual.[11] Because intermediate stage HCC includes both Child-Turcotte-Pugh (CTP) class A and B patients, ascertaining the optimal treatments for these patients still remains a substantial challenge. Recent advances in liver surgery make the resection of intermediate stage HCC possible.[12–15] It is therefore important to clarify the optimal and effective therapy for intermediate stage HCC patients. The purpose of our study was to compare the long-term survival of intermediate stage HCC patients treated with surgical resection or TACE.

2. Materials and methods

2.1. Patients

A total of 210 newly diagnosed intermediate stage HCC patients, including 67 patients (31.9%) with surgical resection and 143 patients (68.1%) with TACE, were retrospectively enrolled from Ren-Ai Branch, Taipei City Hospital between January 1998 and May 2013. The liver function reserve was assessed by the Child-Turcotte-Pugh (CTP) score.[16] The diagnosis of HCC was histologically confirmed in all patients receiving surgical resection and 87 (60.8%) of patients with TACE treatment. The remaining 56 (39.2%) patients with TACE treatment were confirmed by typical imaging exhibited through arterial enhancement and portal venous washout on multiphasic computed tomography (CT) or magnetic resonance imaging (MRI).[4,5] According to the BCLC staging system, the intermediate stage HCC was defined as CTP class A and B cirrhotic patients with large or multifocal HCC who do not have cancer-related symptoms and do not have macrovascular invasion or extrahepatic spread.[8] Treatment for intermediate HCC was guided by a multidisciplinary model (Fig. 1). In the weekly multidisciplinary conference, all patients were discussed, and their eligibility for surgical resection or TACE was evaluated based on images, laboratory analyses and medical history. This study protocol was approved by the institutional review board of Taipei City Hospital.

2.2. Biochemical and serological testing

The biochemical tests were measured using routine automated methods. The HBsAg and anti-HCV were assayed using commercial kits (General Biological HBsAg RIA, General Biological Cooperation, Taiwan. HCV EIA II. Abbott Laboratories, North Chicago, IL, USA).

2.3. Procedure of surgical resection

Indications for surgery were: 1) CTP classification grade of A or B, 2) performance status test was grade 0 or 1, 3) solitary or multiple tumors which were clinically resectable, or 4) the presence of appropriate residual liver volume.[17] Intraoperative ultrasound was routinely performed to determine tumor location and precise definition of tumor–vessel relationship. Anatomic segmental resections were performed for potentially curative operation. Additionally, the resection margin was more than 1 cm.

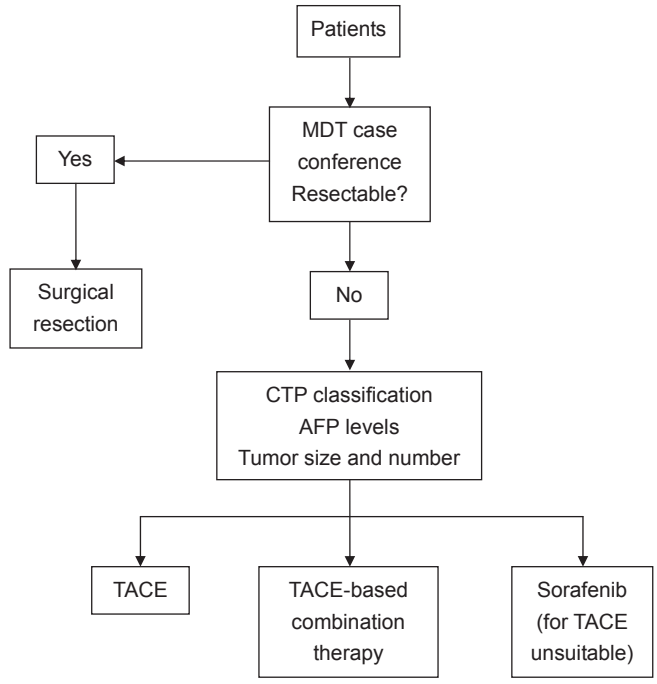

Fig. 1. Ren-Ai multidisciplinary model for treatment of intermediate stage HCC.

2.4. Procedure of TACE

The standardized procedure of TACE was described previously.[18] In brief, TACE procedures were performed in a dedicated angiography suite DFP8000D (Toshiba Medical Systems, Otawara, Japan) with 4Fr J-Curve catheters (Terumo Medical Corporation, Tokyo, Japan) inserted via the right external femoral artery puncture, guided by a matching mandrel (Terumo Medical Corporation, Tokyo). The J-Curve catheter tip was placed in the celiac axis orifice, and one set of digital subtraction angiography was performed. For patients with S5 or S6 tumors which might draw their tumor vessels from superior mesenteric branches, a set of digitally-subtracted superior mesenteric angiography was also performed. If the tumor stains and the supplying vessels were not well-demonstrated by the above angiograms, further superselective angiograms were performed including angiograms of the common hepatic artery, proper hepatic artery, right or left hepatic arteries, and sometimes even the smaller segmental branches. Embolization was performed from the appropriate site, which usually was the proper hepatic artery for multiple bilateral tumors, and the right or left hepatic arteries for unilateral tumors. The embolization agents were ethiodized oil Lipiodol® (Guerbet, Villepinte, France) and absorbable gelatin sponge Surgifoam® (Ethicon, Somerville, NJ, USA), and the chemotherapy agents were mitomycin and doxorubicin. The dosage of lipiodol and gelatin sponge was based on a