ORIGINAL ARTICLE

Chemoembolization outcomes for hepatocellular carcinoma in cirrhotic patients with compromised liver function

David P. Dorn[1], Mary K. Bryant[1], Jessica Zarzour[2], J. Kevin Smith[2], David T. Redden[3], Souheil Saddekni[2], Ahmed Kamel Abdel Aal[2], Stephen Gray[1], Jared White[1], Devin E. Eckhoff[1] & Derek A. DuBay[1]

[1]Liver Transplant and Hepatobiliary Surgery, [2]Department of Radiology, and [3]Biostatistics Division, School of Public Health, University of Alabama at Birmingham, Birmingham, AL, USA

Abstract

Background: Transarterial chemoembolization (TACE) is recommended as a treatment for unresectable hepatocellular carcinoma (HCC) in patients with normal underlying liver function. The efficacy of TACE in cirrhotic patients with compromised liver function is unknown.

Methods: All 'first' TACE interventions for HCC performed at a single institution from 2008 to 2012 were retrospectively reviewed (n = 190). Liver function was quantified via the Child's score. Tumour necrosis after TACE was quantified via the mRECIST criteria.

Results: The 'first' TACE procedures of 100 Child's A and 90 Child's B/C cirrhotic patients were evaluated. As expected, the lab-model for end-stage liver disease (MELD) score was significantly higher in the Child's B/C group. Although the number of tumours were similar between the groups, both the size of the largest tumour and the total tumour diameter were greater in the Child's A group. There were no significant differences in post-TACE tumour necrosis between groups. The median survival after TACE was significantly longer in the Child's A compared with Child's B/C patients (21.9 versus 13.7 months, P = 0.03).

Conclusions: TACE appears to be equally efficacious in cirrhotic patients regardless of their Child's classification based upon equivalent mRECIST measures of tumour necrosis. However, inferior survival after TACE was observed in the Child's B/C group.

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Correspondence

Derek A. DuBay, Liver Transplant and Hepatobiliary Surgery, University of Alabama at Birmingham, 701 ZRB, 1530 3rd Avenue South, Birmingham, AL 35294-0007, USA. Tel: + 1205 996 5970. Fax: + 1205 996 9037. E-mail: ddubay@uabmc.edu

Introduction

Transarterial chemoembolization (TACE) is the standard of care for intermediate stage hepatocellular carcinoma (HCC) in patients that are not candidates for surgical resection or tumour ablation.[1,2] Population-based data demonstrates that TACE is the most common oncological treatment performed for HCC among Medicare patients in the United States.[3] Review of the Scientific Registry of Transplant Recipients (SRTR) data on liver transplantation for HCC also demonstrates that TACE is the most common bridging therapy offered to >70% of patients on a waiting list in the US.[4] Current practice guidelines from the American Association for the Study of Liver Disease (AASLD) recommend TACE 'as "first" line non-curative therapy for non-surgical patients with large/multifocal HCC who do not have vascular invasion or extrahepatic spread. . . .'[5,6] The AASLD's recommendation, however, only apply to Child–Pugh class A patients.[5,6] The AASLD further states that 'patients with advanced liver disease (Child–Pugh class B or C) and/or clinical symptoms of end-stage cancer should not be considered for these treatments as they have an increased risk of liver failure and death.'[5,6]

The AASLD practice guidelines for TACE were based upon a heterogeneous collection of clinical studies, many of which

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utilized non-selective lobar chemoembolization approaches.[7,8] Often, there is significant 'innocent bystander' hepatocyte necrosis as a complication of non-selective lobar chemoembolization approaches.[9,10] There is increasing recognition that selective HCC chemoembolization approaches, where only the hepatic arterial branches directly supplying the HCC are treated, may be performed with minimal (non-targeted) collateral damage to adjacent uninvolved hepatic parenchyma.[10] The development of microcatheters and the application of super-selective embolization techniques have prompted the University of Alabama at Birmingham (UAB) Liver Tumor Board to increasingly offer TACE to select cirrhotic patients with compromised liver function.

The purpose of this study was to measure the safety and efficacy of TACE procedures performed as first-line therapy in cirrhotic patients with Child–Pugh class B or C compromised liver function. The outcomes in the Child–Pugh B or C patients were compared with a contemporaneous group of Child–Pugh A cirrhotic patients treated similarly. Our hypotheses were (i) TACE can be performed safely in Child–Pugh B or C cirrhotic patients, (ii) there will be no difference in HCC tumour necrosis in Child–Pugh A compared with Child-Pugh B or C patients and (iii) there will be equivalent post-TACE survival in Child–Pugh A compared with Child–Pugh B or C patients.

Methods

Ethics approval for this study was obtained from the University of Alabama Institutional Review Board (Protocol #X100310006). A retrospective chart review was performed for all patients receiving a TACE at UAB between January 2008 and June 2012. Patients were identified from an internal TACE database that is used for clinical purposes.

Patient population

Patients were diagnosed with HCC according to the AASLD criteria either by biopsy or by the presentation of classic HCC radiological features of a >2-cm hypervascular lesion arising in the setting of cirrhosis with arterial phase enhancement and portal venous phase washout.[11] The decision to offer TACE to patients with HCC was made by a multi-disciplinary liver tumour board at UAB including medical oncologists, surgeons, hepatologists and interventional radiologists. Candidacy for TACE in Child–Pugh A patients was determined by established AASLD practice guidelines.[5,6] Select Child–Pugh class B and C cirrhotic patients were offered TACE if they had an ECOG functional status of 0 or 1, limited tumour burden and medically controlled symptoms of hepatic decompensation. There was no absolute cut-off model for end-stage liver disease (MELD) score, Child–Pugh score, bilirubin, international normalized ratio, etc. However, most Child–Pugh class B and C patients offered TACE had a hyperbilirubinemia that was predominantly indirect and/or hypoalbuminemia out of proportion to the overall clinical assessment. Patients could have ascites although the ascites needed to be controlled with diuretics; an active need for paracentesis was a contraindication. Patients could also have a history of encephalopathy but this needed to be controlled medically without evidence of recent hospitalizations. Child–Pugh class B or C patients were not offered TACE if they had medically refractory ascites or poorly controlled encephalopathy.

A list of all patients treated with TACE between January 2008 and June 2012 was generated from the UAB Interventional Radiology procedures electronic database (n = 348). Patients were excluded if they had a non-HCC tumour type (n = 45) and if the TACE procedure performed was not the 'first' TACE intervention (n = 113) (Fig. 1). HCC tumours that had previously been treated operatively or with another locoregional therapy such as radiofrequency ablation or external beam radiotherapy were excluded from the study. Patients taking chemotherapeutic agents before and/or after the procedure were included in the study. All patients were felt to have cirrhosis based upon a combination of platelet counts and radiographical criteria.

Imaging

Patients were only included if they had high-quality three phase or four phase computed tomography imaging or liver protocol magnetic resonance imaging (MRI) within 75 days prior to and after the TACE procedure.

HCC tumour assessment and post-TACE tumour necrosis quantification

After an extensive training period, two second year medical students (D.D. and M.B.) independently reviewed CT and MRI studies performed before and after TACE for all patients. The body radiology fellow (J.Z.) taught the medical students about the basics of multiphasic CT and outlined a consistent approach to calculating axial tumour dimensions and identifying post-TACE tumour necrosis. After these teaching sessions, the fellow and medical students jointly worked through 20 patients together. The medical students, body fellow and senior staff then reviewed 20 patients independently and the results were reviewed to verify consistency. The medical students then reviewed all CT imaging independently. The medical students saved the marked images indicating caliper and contrast enhancement measurements. The UAB body radiology fellow independently reviewed all CT and MRI studies and confirmed all measurements. A staff radiologist (K.S.) with 19 years of experience in body imaging confirmed all quantitative data. When evaluating the cross-sectional imaging, the assessors were blinded to the Child–Pugh class and MELD score.

The tumour response was assessed via the modified response evaluation criteria in solid tumours (mRECIST). Using CT or MRI studies obtained prior to the procedure, a pre-TACE tumour size was determined. The measurements were then repeated on CT or MRI studies obtained after the procedure. Consistent with mRECIST criteria, only axial images were used for tumour size