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ORIGINAL ARTICLE

Surgical management of hepatocellular carcinoma within and beyond BCLC indications in a middle volume center

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KEYWORDS
Liver cirrhosis;
Liver surgery;
Barcellona Clinic Liver Cancer Classification;
Hepatocellular carcinoma

Summary
Aim of the study: Current criteria for hepatic resection in patients with hepatocellular carcinoma (HCC) according to Barcellona Clinic Liver Cancer (BCLC) classification is debated. Actually, patients with multinodular or large HCC > 5 cm are excluded from surgical treatment following the algorithm, but several studies from referral centers showed that such patients may benefit from surgical resection in the clinical practice. The aim of this study was to compare short- and long-term outcomes after liver resection for HCC in stage 0/A or B in a middle volume center.
Patients and methods: Patients were grouped according to BCLC classification. Postoperative mortality, morbidity, overall and disease-free survival, univariate analysis of prognostic factors on survival was analyzed.
Results: Among 66 surgical procedures in 64 patients included in the study, 41 were BCLC stage 0/A (62.1%) and 25 BCLC stage B (37.9%). The overall 30- and the 90-days mortality rates were 1.5% and 3%. Patients in BCLC stage B had higher transfusion rate ($P = 0.04$) but similar morbidity and mortality compared to patients in BCLC stage 0/A. After a median follow-up of 35 months (range: 14—147), the overall survival at 1, 3 and 5 years resulted 95%, 61.1%, 46.2% for stage 0—A and 83.3%, 50%, 41.2% for stage B ($P = 0.73$). Univariate analysis identified poorly differentiated tumors ($P = 0.02$) and positive margin ($P = 0.02$) as negative prognostic factors on survival.
Conclusions: Surgical treatment of HCC in BCLC stage B offers similar results than the ones in BCLC stage 0/A and consequently should not be considered contraindicated for such patients.

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Introduction

Hepatocellular carcinoma (HCC) is the main common primary tumor of the liver, representing approximately 85—90% of primary hepatic malignancies and is usually associated with cirrhosis [1]. Surgical resection of HCC should balance oncological radical principles with minimization of organ damage. In this sense, liver transplantation is considered the gold standard treatment, because offers the possibility to treat simultaneously the liver cancer and the damaged organ. On the other hand, organ shortage restricts indications to liver transplantation, addressing many patients to receive local therapies [2]. Several HCC staging systems based on tumor features and liver function have been proposed to guide therapeutic decisions. Barcelona Clinic Liver Cancer (BCLC) classification has been approved as guidance for HCC treatment algorithms by the European Association for the Study of Liver (EASL) and the American Association for the Study of Liver Disease (AASLD), because of its ability to categorize patients into recommended therapeutic options [3,4]. The BCLC staging system currently recommends curative treatments for very early- or early-stage HCC (BCLC stage 0-A), palliative therapies such as transarterial chemoembolization (TACE) for intermediate-stage HCC (BCLC stage B), sorafenib administration for advanced stage HCC (BCLC stage C), and supportive care for end stage HCC (BCLC stage D) [5]. According to the algorithm, hepatic resection should be performed only in patients with small single tumors without signs of portal hypertension or hyperbilirubinemia [5].

By contrast, several studies from referral hospitals for surgical treatment of HCC have shown that hepatic resection can lead to good short- and long-terms outcomes even in patients without indication according the BCLC indications, as in patients with portal hypertension and with multinodular or large HCC [6—8]. Moreover, some authors reported that liver resection can provide better survival benefit than TACE in patients in BCLC stage B patients [9]. Consequently, the identification of the best treatment modality for patients in BCLC stage B is still debated, and a main argument explaining the reticence to enlarge surgical indication beyond BCLC indications could be related to the safety of surgical outcomes and reproducibility of such results outside of referral centers. The aim of the present monocentric study was to compare short and long term outcomes of patients undergoing surgical resection for HCC in stage 0/A or stage B in a middle volume center.

Methods

Study design and data collection

From 1st January 2005, we recorded data of all patients undergoing hepatic resection at our hospital. From this prospective database, we retrospectively selected patients with the following characteristics: HCC in stage 0, A or B according to BCLC staging system operated on up to 30th June 2014. The study was performed as intention to treat analysis.

Since the creation of a multidisciplinary team in 2011, the cases were discussed in meetings involving surgeons, hepatologists, pathologists, radiologists, interventional radiologists and oncologists; prior to 2011, cases were evaluated by surgeons and hepatologists, but out of structured multidisciplinary meetings. In all the patients included in the study liver, transplantation was contraindicated because of patient's age or tumor features. San Gerardo has not a liver transplant team into the hospital; our multidisciplinary group has an established partnership with a transplant team present in another hospital and we used to refer patients with indication to LT to such team. All patients have been studied for clinical history, radiologic imaging, laboratory tests, histopathological and surgical reports. Besides, patients were analyzed in terms of long-term survival, as a whole population.

Study endpoints

The end point of this study was to analyse postoperative short- and long-term outcomes of the entire population and compare patients stratified by the BCLC classification as class A/0 versus B. As short-term outcomes we selected the rate of postoperative complications and 30-day and 90-day mortality and as long-term outcomes, the overall survival (OS) and the disease free survival (DSF) in the whole population and in the sub-groups stratified following the BCLC classification (BCLC 0/A and BCLC B). Furthermore, potential prognostic factors for survival were analyzed.

Definitions

Terminology for liver anatomy and resection was based on the Brisbane classification [10]. The severity of postoperative morbidity was defined using the Dindo-Clavien classification [11].

Preoperative management

Patients were first assessed and studied by clinical history, underlying liver disease and related aetiology, as well as any previous HCC treatment such as radiofrequency (RF) ablation, percutaneous ethanol injection (PEI), TACE or hepatic resection. Preoperative imaging workup included abdominal ultrasonography (US), computed tomography (CT) and in some cases magnetic resonance imaging (MRI). Patients were considered for surgical resection if the hepatic functional reserve classified by the Child-Pugh scoring was class A or B7. Concomitant ascites was considered an absolute contraindication to surgery. The presence of portal hypertension, defined by oesophageal varices, splenomegaly with platelet count < 100,000 mm^3 or hepatic venous pressure gradient > 10 mmHg, was not considered an absolute contraindication to surgery.

Follow-up

Patients were followed up at the hepathology centre of the San Gerardo Hospital by office visits every 3—6 months. Follow-up of patients was based on physical examination, liver function test, tumor markers and radiological imaging tests such as US, MRI and CT.

Statistical analysis

Descriptive statistics for continuous data were expressed as mean ± SD as well as median (range). Discrete data were summarized as numbers and percentages. For continuous variables, the *t*-test or the Mann—Whitney test were used, depending on normality distribution assumption. For categorical variables the χ^2 test or the Fisher's exact test as

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