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REVIEW ARTICLE

Mini-review. Liver transplantation for hepatocellular carcinoma

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KEYWORDS
Chronic hepatitis C;
End stage liver disease;
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Cirrhosis

Abstract Liver transplantation is the gold standard treatment for end stage liver disease, including patients with cirrhosis and hepatocarcinoma falling within Milan criteria. HCC is the sixth most common cancer around the world, and leading cause of death among cirrhotic patients. Diagnosis is based upon radiological characteristics and rarely biopsy results; the Barcelona Clinic Liver Cancer staging system is the most used guideline for treatment. With several treatment options available transplantation and resection continue to be the major curative therapeutic option for this patients. However treatment must be individualized to each patient to improve recurrences and outcomes. The aim of this paper is to review the present role of liver transplantation in the management of hepatocarcinoma.

PALABRAS CLAVE
Hepatitis C crónica;
Recurrencia;
Enfermedad hepática no alcohólica;
Cirrosis;
Enfermedad hepática terminal

Mini-revisión. Transplante hepático para carcinoma hepatocelular

Resumen El trasplante hepático es el estándar de oro en el tratamiento de enfermedad hepática avanzada, incluyendo pacientes cirróticos que han desarrollado hepatocarcinoma pero que se encuentran dentro de los criterios de Milán. El hepatocarcinoma es el sexto tumor más común alrededor del mundo y es la principal causa de muerte en pacientes cirróticos. El diagnóstico se basa principalmente en las características radiológicas del tumor y raras veces en resultados de patología. El sistema de estatificación desarrollado por el Clinic de Barcelona es la guía más usada para el tratamiento. Existen diferentes opciones terapéuticas para el hepatocarcinoma; sin embargo, el trasplante y la resección quirúrgica siguen siendo la opción curativa

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con mejores resultados. El tratamiento debe de ser individualizado para cada paciente con el fin de mejorar los resultados y minimizar recurrencias. El objetivo de este artículo es revisar el rol actual del trasplante hepático en el manejo del hepatocarcinoma.

Introduction

Hepatocellular carcinoma (HCC) is the sixth most common cancer worldwide and the third most frequent cause of cancer-related death.[1] It's incidence is rising in western countries, usually occurs in the setting of chronic liver disease and cirrhosis. With more tight surveillance programs the diagnosis of this type of cancer has been earlier in the natural history of this disease, which means increased curative treatments and better survival rates.

There are several staging and treatment modalities for HCC although the mainstay of treatment is surgical resection; the majority of patients are not eligible because of tumor extent or underlying liver function. Underlying liver disease may limit any therapy; Nowadays hepato-pancreato-biliary surgery and liver transplantation programs choose de Barcelona Clinic Liver Cancer (BCLC) staging system to guide treatment decisions. Some selected group of patients may benefit from liver transplantation (LT).

The aim of this paper is to review the present role of liver transplantation in the management of HCC.

Etiology

Chronic infections of hepatitis B virus (HVB) and hepatitis C virus (HVC) are responsible for nearly 78% of cases of HCC worldwide.[2] However there are other potential risk factors for HCC such as alcoholic cirrhosis with an annual risk of 1%.[3] Obesity and diabetes are also risk factor for HCC in patients with non-alcoholic steatohepatitis (NASH) and fatty liver disease (FLD); 20% of patients with NASH progress to liver fibrosis and ultimately in 3% cirrhosis.[4]

Other risks factors for HCC include: hemochromatosis, biliary disease such as primary cholangitis and primary biliary cholangitis, liver adenomas (risk for malignant transformation is 10%).[5] Some toxins such as aflatoxin produced by *Aspergilus flavus* can be associated to HCC; finally tobacco use is an independent risk factor of HBV or alcohol abuse to develop HCC.[6]

Diagnosis, staging systems and therapeutic options

Decades ago the diagnosis of HCC was made in patients with advanced stage disease, treatment was difficult and median survival rates were less than 3 months.[7]

In those days, morbidity associated therapy was high. In recent years with new technologies and surveillance strategies the diagnosis of HCC is done earlier and therefore we can offer curative treatments with 5-year survival rates from 50 to 75%.[8]

The diagnosis of HCC is based on imaging techniques and/or biopsy; the characteristic image on a single dynamic contrast-enhanced CT technique shows intense arterial uptake followed by ''washout'' of contrast in the venous-delayed phases makes the diagnosis.[9] As the patient undergo for initial evaluation with contrast-enhanced TC, this also serves to rule out extrahepatic spread or macrovascular involvement, that could contraindicate transplantation.

Regarding on biopsies, their interpretation and distinction between high-grade dysplastic nodules and HCC is challenging, experienced pathologists tend to confirm their diagnosis by staining for glypican 3, heat shock protein 70 and glutamine synthetase, the positivity of two of these stains confirms HCC.[10]

Since the diagnosis is made on the basis of cirrhotic patients the aim of surveillance is to improve outcomes and decrease mortality rates, the most used tests for screening are alfa-fetoprotein (AFP) and liver ultrasound (US) the sensitivity is 87% and 75% respectively when used alone. Both are confirmatory tests. The current recommendation of the American Association for the Study of Liver Disease (AASLD) is an interval of 6 months surveillance in patients with high risk using US.[11]

Once HCC is diagnosed the next step is staging. Among many staging systems developed worldwide the BCLC staging system is the most useful to guide treatment decision. (Fig. 1)

According with published results, this staging system allows an estimation of life expectancy. One of the most useful characteristics of this system is the identification of patients with early HCC potentially curable, those that may benefit from LT and those in terminal stage that could not benefit from any medical or surgical treatment.[12,13]

Therapeutic options for HCC includes: surgical resection, liver transplantation, radiofrequency ablation (RFA), microwave ablation, percutaneous ethanol or acetic acid ablation, trans arterial chemoembolization (TACE), radioembolization, cryoablation, radiation therapy and stereotactic radiotherapy, systemic chemotherapy and molecularly targeted therapies.

Surgical resection is the best curative treatment of HCC, offering a 5-year survival rate of 60–70%.[14] However in this review we will focus on LT.

Liver transplantation

Liver transplantation is an attractive option in patients with cirrhosis, end stage liver disease and HCC, because in the same procedure the tumor can removed meanwhile replacing the cirrhotic liver.

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