Best Practice & Research Clinical Gastroenterology 26 (2012) 531–548

Contents lists available at SciVerse ScienceDirect

Best Practice & Research Clinical Gastroenterology

14

Liver transplantation in the setting of chronic HCV

Norah Terrault, MD, Professor of Medicine *

University of California San Francisco, United States

Keywords:
Recurrent cirrhosis
Cholestatic hepatitis
Donor age
IL28B
Liver biopsy
Elastography
Peginterferon
Ribavirin
Protease inhibitors

A B S T R A C T

Recurrent HCV disease is the most common cause of graft loss and patient mortality in HCV-infected liver transplant (LT) recipients. Risk factors for more severe recurrence that are potentially modifiable are older donor age, prolonged cold ischaemia time, prior treated acute rejection, CMV hepatitis, IL28B donor genotype, and post-LT insulin resistance. The most effective means of preventing HCV recurrence is eradicating HCV prior to LT. Select wait-list candidates with compensated or mildly decompensated disease can be considered for antiviral treatment with peginterferon, ribavirin (and protease inhibitor if genotype 1). For the majority of LT patients, HCV treatment must be delayed until post-transplant. Treatment is generally undertaken if histologic severity reaches grade 3 or 4 necroinflammation or stage $\geq$2 fibrosis, or if cholestatic hepatitis. Achievement of sustained viral response (SVR) post-LT is associated with stabilization of fibrosis and improved graft survival. SVR is attained in ~30% of patients treated with peginterferon and ribavirin. Poor tolerability of therapy is a limitation. Combination therapy with telaprevir or boceprevir added to peginterferon and ribavirin is anticipated to increase efficacy but with higher rates of adverse effects and challenges in managing drug–drug interactions between the protease inhibitors and calcineurin inhibitors/sirolimus.

Introduction

Chronic hepatitis C is an important cause of cirrhosis and hepatocellular carcinoma globally. In the United States, like to other countries in the Western world, HCV is the most common indication for liver transplantation (LT) and in recent years, the proportion of patients with hepatocellular carcinoma

* Tel.: +1 415 502 0318; fax: +1 415 476 0659.
E-mail address: norah.terrault@ucsf.edu.

1521-6918/$ – see front matter © 2012 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.bpg.2012.09.010

(HCC) as the primary indication for LT has increased, likely reflecting changes in prioritization of small HCC for LT as well as a true increased prevalence of HCC in the HCV-infected population [1].

The overall 5-year graft and patient survival rates are 23% lower in HCV-infected LT recipients compared to non-HCV infected recipients [2] (Fig. 1). Successful eradication of HCV infection with pre-transplant and post-transplant antiviral therapy improves graft outcomes [3,4]. However, current antiviral therapy is limited by poor tolerability in wait-listed patients, and low efficacy as well as higher risk of adverse events in the post-transplant population [5]. Thus, identification of modifiable donor, recipient and post-LT cofactors that influence fibrosis progression and risk of graft loss have been critically important.

Natural history

Spontaneous clearance of HCV post-transplantation has been described but is a rare event. For most patients recurrent viraemia is detectable within days post-transplant [6,7]. On average, HCV RNA levels are approximately 1-$\log_{10}$ higher post-transplant compared to pre-transplant. Histologic evidence of recurrent disease is present in the majority of patients at one-year post-LT and 11–37% have moderate fibrosis (stage 2 on scale of 4) at this timepoint [8,9]. Approximately 10% develop severe early recurrence with cholestatic features within the first year (usually within the 6 months) post-transplantation, which can rapidly progress to graft loss if untreated [16]. Fibrosis progression is not linear; the rate of fibrosis progression is faster at higher stages of fibrosis and with reduced time in a given stage of fibrosis [10,11]. The median time to recurrent cirrhosis is 8–10 years [12], but 'rapid progressors' develop recurrent cirrhosis within 3–5 years [9]. Once cirrhosis is diagnosed, the risk of decompensation is 30–42% within the following year [13–15]. Once decompensated cirrhosis occurs, the risk of death is high in the absence of retransplantation, with ~60% dying within a year of their first decompensating event.

Predictors of fibrosis progression and implications for management

Recipient, donor and transplant-related factors contribute to the risk of recurrent cirrhosis and graft loss (Table 1). While there is often limited capacity to change recipient and donor factors to improve post-LT outcomes, transplant-related factors differ in that they are frequently modifiable (Table 2).

Recipient factors

Higher rates of severe HCV disease and reduced graft survival are associated with female gender, African-American race, and HIV coinfection. Older age has been associated with reduced survival but

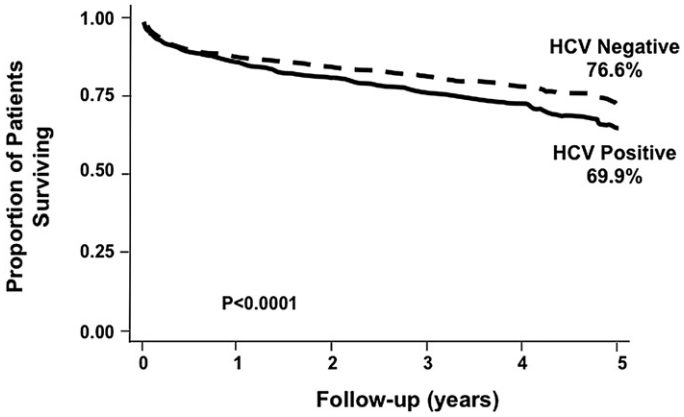

Fig. 1. Patient survival of U.S. adult liver transplant recipients with and without HCV. Patients transplanted for HCV-related liver disease had a 23% increased risk of death and a 30% increased risk of graft loss at five years when compared to patients transplanted for non-HCV etiologies. Source (adapted): [2].