

## Have All the Questions Regarding the HCV Infection in Renal Transplant Recipients been answered?

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Hepatitis C virus (HCV) infection seems to be the most important cause of chronic liver disease in renal transplant recipients (RTRs) (1). The reported prevalence of anti-HCV antibodies is wide ranging among RTRs living in different countries and geographic regions from 2.6 to 66% (1-3). HCV infection is a common cause of chronic hepatitis in patients with end-stage renal disease (ESRD) (4).

The effect of pretransplant HCV infection on the outcome of renal transplantation is controversial and the impact of HCV infection on patient survival following it has been a subject of debate. However, some studies have shown that there is an increased risk of mortality among the recipients with a positive anti-HCV antibody before transplantation (5, 6). Chronic hepatitis, cirrhosis, and hepatocellular carcinoma are well-known hepatic complications of HCV, especially after renal transplantation (7, 8). Importantly, liver dysfunction is an important cause of morbidity and mortality among RTRs and liver failure has been reported as a cause of death in 8–28% of long-term survivors following renal transplantation (5, 9-14). Nevertheless, some studies have shown better survival in HCV-positive RTRs than in similar HCV positive patients on dialysis (15).

HCV infection in immunocompetent hosts is indolent and causes a slowly progressive liver dysfunction (16). However, data on natural history of HCV infection in RTRs are conflicting (16).

Furthermore, the viral load increases during immunosuppressive therapy (17). However, little is known about the natural history of HCV infection during long-term treatment with immunosuppressive drugs. In addition, the effect of HCV infection on patient and graft survival is controversial (13). On the other hand, the long-term immunosuppressive therapy in RTRs might have harmful effects upon the liver function as reported in non-renal disease individuals (13). Moreover, it has illustrated an HCV RNA-positive carrier with normal liver enzyme tests and a relatively benign course during the first decade after renal transplantation (13). In addition, some authors believe that HCV infection does not adversely affect patient and graft medium-term survival in RTRs (14, 18), and it has been suggested that fewer than 10% develop advanced fibrosis even 10 years after infection (2, 16). However, the survival rate of HCV-positive recipients appears to decrease gradually over the long term, especially beyond a decade following transplantation (13, 19). That the graft survival is lower in HCV-positive patients may seem logical, primarily because of the possibility of progression of liver disease and greater prevalence of diabetes and proteinuria (17).

Eradication of HCV before renal transplantation is rational and treatment with interferon (IFN) should be considered in HCV-infected patients undergoing dialysis who are on the waiting list. Post-renal

transplant treatment of HCV infection is not routinely recommended due to the potential increased risk of acute rejection (20-24). However, there are some reports of benefit from treatment of HCV infection, IFN monotherapy or combination therapy with IFN plus ribavirin (25, 26).

Finally, the questions below should be considered for the researches in future.

What is the role of HCV viral load in the follow-up of the patients after renal transplantation? Is survival of HCV infected-hemodialysis patients less than RTRs? What is the impact of earlier renal transplantation on patient survival? Is screening of hepatocellular carcinoma mandatory for increasing of the patient survival among HCV-infected RTRs? The importance of proteinuria in patient survival and the effect of diabetes on graft and patients survival need more data. The optimal immunosuppressive regimen in this group of patients remains uncertain and the optimal treatment of hepatitis C infection after kidney transplant is unclear (27) and requires additional agents or alternative therapeutic approaches and further studies (28).

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