

tastatic disease include LE and abdominoperineal resection (APR) with or without inguinal and pelvic lymphadenectomy followed by adjuvant radiotherapy or chemotherapy. Wide LE followed by adjuvant radiation produces equivalent five-year survival to that of APR (2,6,7). However, improved

local control for large lesions and long-term survival for lesions smaller than 2 mm are seen after APR (7). No systemic chemotherapy regimen for metastatic ARM is the standard of care. In conclusion, primary ARM is a rare, aggressive malignancy with a poor prognosis.

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Ansley S. THARPE¹, Kenneth J. VEGA²,
Bruce W. TROTMAN³

University of Florida/Jacksonville, ¹Division of Gastroenterology, Jacksonville, FL, USA

University of Oklahoma, ²Division of Digestive Diseases, Oklahoma City, OK, USA

³University of Maryland, School of Medicine, Baltimore, MD, USA

Acquisition time: A key point of hepatitis C virus-related liver disease in renal transplant recipients

Renal transplant alıcılarında hepatit C virüsü ile ilişkili karaciğer hastalığında anahtar bir nokta: Enfeksiyonu edinme zamanı

To the Editor,

I read with great interest the article entitled "The impact of hepatitis C virus infection on long-term outcome in renal transplant patients" by Ruhi Ç, et al. (1) that highlights the impact of hepatitis C virus (HCV) infection on long-term outcome in renal transplant (RT) recipients. To address this aim, the investigators conducted a retrospective study among 1811 patients who received RT between 1999 and 2009 in Akdeniz University Organ

Transplantation Center. One hundred patients (5.5%), all of whom acquired the infection during the pre-RT period, were found to be HCV-seropositive. For a median follow-up of 35.7 months, graft survival was lower in anti-HCV-positive patients, but patient survival was similar between the anti-HCV-positive and -negative groups. As the authors pointed out, the apparently higher rate of graft loss in the anti-HCV-positive patients could

Address for correspondence: İlker TURAN

Department of Gastroenterology, Ege University, School of Medicine, İzmir, Turkey
E-mail: ilkerturan@gmail.com

Manuscript received: 25.07.2011 **Accepted:** 09.01.2012

doi: 10.4318/tjg.2012.0466

be due to the higher number of cadaveric transplants in this group. Transaminase elevation was observed in 27% of patients with HCV infection, but none of them developed liver failure or cirrhosis.

Chronic HCV infection is emerging as the most important cause of liver disease in patients with end-stage renal disease (ESRD). Given that the use of ribavirin is currently contraindicated in this population (ribavirin is excreted through the kidney and not cleared by dialysis), and clearance of interferon is lower in patients on dialysis compared with those who have normal renal function, an optimal therapy for hepatitis C before RT remains a challenge.

Controversy exists as to the impact of HCV infection on patient or graft survival and the progression of liver disease in RT recipients. Several studies have shown that the presence of HCV infection before RT does not appear to have any unfavorable effect on patient or graft survival for 5–8 years (2,3); however, other investigators have reported conflicting results (4,5).

For the first time, we have shown that the clinical and histopathological course of HCV infection in RT patients appears to be related to the acquisition time of the infection (6). In our study, a total of 197 patients who had undergone RT between 1992 and 1998 at the Ege University Organ Transplantation and Research Center were divided into three groups, including the pre-RT HCV group (n=47 patients), post-RT HCV group (n=27 patients), and control group (both anti-HCV and HCV RNA were negative during the pre- and post-RT period, n=123 patients). Details of the methodology of the study can be found in the relevant reference (6). After a mean follow-up of 7.1 ± 4.0 years, ascites and encephalopathy were seen only in the post-RT HCV group. Among the patients in whom liver biopsy was performed, histological grade and

stage were significantly higher in patients with post-RT HCV infection (37% of those had advanced stage [stage 3-4]) compared to those with pre-RT HCV infection (96% of those had mild to moderate stage [stage 0-1-2]). Cirrhosis occurred in 25% of patients in the post-RT HCV group, whereas no patients with pre-RT HCV infection had cirrhosis at the time of their liver biopsy ($p=0.005$). Three patients in the post-RT HCV group died due to liver failure. Five- and 10-year death-censored graft-survival rates were lower in the pre- and post-HCV groups than the control group, but non-significant for pre-RT HCV vs. post-RT HCV groups. Five- and 10-year patient survival rates between the three groups were similar.

Our study has clearly indicated that liver damage can occur at an accelerated rate, leading to cirrhosis, in patients who acquired HCV infection in the peri- or postoperative period, unlike the indolent course of infection seen in pre-RT anti-HCV-positive patients. The exact mechanism of this effect is not known. It has been reported that risk of chronic liver disease and liver failure-associated mortality were increased in recipients transplanted from anti-HCV-positive donors. De novo HCV infection characterized by severe hepatitis and high mortality rate was also described in heart transplant patients (7,8). Overall, these data indicate that HCV infection, transmitted at the time of transplantation, can lead to more severe liver disease in renal and in non-renal transplant patients, though the effect on patient survival is not clear.

In closing, the American Gastroenterological Association (AGA) has recommended that if an HCV-positive patient with ESRD is a candidate for RT, the degree of hepatic fibrosis should be evaluated because advanced fibrosis and cirrhosis in these individuals are associated with an increased risk of graft and patient loss (9).

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İlker TURAN

Department of Gastroenterology, Muğla State Hospital, Muğla

Tissue inhibitor of metalloproteinases-1, hyaluronan and chronic hepatitis

Metalloproteinazlar-1 doku inhibitörü, hyaluronan ve kronik hepatit

To the Editor,

We read with great interest a recent report on “serum connective tissue markers as predictors of advanced fibrosis in patients with chronic hepatitis B and D” (1). According to this work, tissue inhibitor of metalloproteinases-1 and hyaluronan were powerful predictors, and Seven et al. (1) proposed that “advanced liver fibrosis in chronic hepatitis B and D may be predicted” based on these two biomarkers. Apart from simple problems regarding the small number of subjects and lack of data on quality control of the test, there are some issues to

be discussed. There are some previous reports on the diagnostic properties of tissue inhibitor of metalloproteinases-1 and hyaluronan. It should be noted that high negative predictive value but low positive predictive value can be seen (2). Thus, these markers should be useful for “ruling out” but not “definitively diagnosing” severe fibrosis. In addition, some other possible confounding diseases such as rheumatoid arthritis and gastric cancer can significantly affect the diagnostic properties of the markers (3,4).

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Somsri WIWANITKIT, Viroj WIWANITKIT

Wiwanitkit House, Bangkhuae, Bangkok, Thailand

Address for correspondence: Somsri WIWANITKIT
Wiwanitkit House, Bangkhuae, Bangkok, Thailand
E-mail: somsriwiwan@hotmail.com

Manuscript received: 21.09.2011 **Accepted:** 31.10.2011

doi: 10.4318/tjg.2012.0445