Impact of Pretransplantation GB Virus C Infection on the Outcome of Renal Transplantation

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Abstract. Among renal transplant recipients with posttransplantation liver disease, the etiology remains unknown in 10 to 16% of patients. The discovery of yet another parenterally transmitted hepatitis virus, GB virus C (GBV-C), has opened avenues to study the prevalence and risk factors for GBV-C infection among patients undergoing renal transplantation and its impact on posttransplantation clinical outcomes. A cohort of 103 randomly selected recipients of kidneys were examined from anti-hepatitis C virus (HCV) (HCV)-negative donors between 1986 and 1990. Pretransplantation sera were available in 99 of 103 (96%) recipients and were tested for anti-HCV, using a second-generation ELISA, and for GBV-C RNA by reverse transcription PCR. Pretransplantation GBV-C RNA was present in 18 of 99 (18%, 95% confidence interval [CI], 17.2 to 18.8%) recipients. GBV-C RNA was present in 5 of 22 (23%) anti-HCV-positive recipients compared with 13 of 77 (17%) anti-HCV-negative recipients (P = 0.53). The median number of pretransplantation blood transfusions among recipients with GBV-C RNA before transplantation was significantly higher than among recipients without GBV-C RNA (10 versus 7, P = 0.05). Posttransplantation liver disease and non-A, non-B hepatitis (NANBH) was observed in 35 and 18%, respectively, of GBV-C RNA-positive recipients compared with 28 and 10%, respectively, of GBV-C RNA-negative recipients. Using Cox regression analysis, the relative risk (RR) of posttransplantation liver disease among recipients with GBV-C RNA before transplantation was 1.37 (95% CI, 0.55 to 3.41), and posttransplantation NANBH was 2.09 (95% CI, 0.64 to 6.79). The RR of graft loss and death were not increased (0.88 and 0.92, respectively). When adjusted for pretransplantation anti-HCV, the RR of posttransplantation liver disease, NANBH, graft loss, and death did not change appreciably. In summary, although a higher risk of posttransplantation liver disease was observed among recipients with pretransplantation GBV-C infection, the analyses presented here do not allow for a precise estimate of this risk. (J Am Soc Nephrol 8: 1164–1173, 1997)

Liver disease is an important cause of morbidity and mortality after renal transplantation (1), and hepatitis C virus (HCV) has been identified as the leading cause of posttransplantation liver disease (2). Although other viral infections (hepatitis B, cytomegalovirus, herpes simplex, and Epstein-Barr virus), drugs and toxins (alcohol, azathioprine, cyclosporine, tacrolimus), and hemosiderosis have been implicated in the majority of remaining cases (3), the etiology remains unknown in 10 to 16% of these patients (4–7).

Similarly, the etiological agent has remained elusive in approximately 10 to 20% of patients with community-acquired and post-transfusion hepatitis (8). The search for other human hepatitis viruses led to the discovery of GB viruses by Simons and colleagues (9,10) in 1995. The group of GB viruses (named after a surgeon from whom the first serum was obtained) consists of three distinct agents: GB virus-A (GBV-A), GB virus B (GBV-B), and GB virus C (GBV-C) (9–11). GBV-A and GBV-B are animal viruses, and GBV-C is a human virus (10). GBV-C has since been shown to contain a single-stranded RNA consisting of 9125 nucleotides coding for 2906 amino acids (12). More recently, Linnen and colleagues reported the cloning of hepatitis G virus (HGV) (13), which appears to be an isolate of GBV-C (14).

The prevalence of GBV-C RNA is 1.7% among healthy volunteer blood donors (13), 8.3% among cadaver organ donors (15), 29% among liver transplant recipients (16), and 33% among intravenous drug abusers (13). Among chronic hemodialysis patients, the prevalence of GBV-C RNA has been reported to be 3.1% in Japan (17) and 55% in Indonesia (18). Transmission of GBV-A and GBV-B has been demonstrated in animals inoculated with infectious serum (19). Although the data on transmission in humans are limited, Linnen and colleagues have reported on two patients who acquired HGV infection after blood transfusion during surgery and subsequently developed hepatitis (13). However, to date, the natural history of GBV-C infection among nonimmunosuppressed or immunosuppressed individuals has not been reported. We report the prevalence of pretransplantation GBV-C infection...
among renal transplant recipients and its impact on posttransplantation clinical outcomes.

Materials and Methods

Study Design

We used a cohort of transplant recipients previously selected to study the impact of pretransplantation HCV infection on posttransplantation clinical outcomes (20). Briefly, 110 of 1051 recipients of kidneys from anti-HCV-negative donors between 1986 and 1990 were randomly selected (20). Sera were available in 103 of the 110 patients. Results of pretransplantation anti-HCV testing (Ortho HCV ELISA 2.0, Raritan, NJ), clinical characteristics, posttransplantation HCV markers, and clinical follow-up until December 1993 have been reported previously (20). Additional pretransplantation sera were available in 99 of the 103 (96%) recipients and were tested for GBV-C RNA by reverse transcription (RT)-PCR at Abbott Laboratories (North Chicago, IL). Information on graft and patient survival was updated until December 1995, and clinical outcomes among GBV-C RNA-positive and -negative patients were compared.

To examine the possibility of transmission of GBV-C infection by organ transplantation, available sera of cadaver organ donors who donated organs to patients testing negative for GBV-C RNA before transplantation, but positive after transplantation, were retrieved and tested for GBV-C RNA.

Clinical Information

As described previously (20), pretransplantation records were reviewed for age, gender, duration since initiation of dialysis, history of liver disease, therapy with hepatotoxic drugs, liver function tests, number of blood product transfusions, pregnancies, previous transplants, and results of serological tests for hepatitis B surface antigen and antibody to cytomegalovirus. Posttransplantation records were reviewed previously to determine the protocol for immunosuppression; episodes of rejection and the type of antirejection therapy; and prevalence, onset, and cause of liver disease, patient and graft survival, and causes of liver disease, graft loss, and death. The cause of each episode of abnormal liver function tests was assessed from all available investigations and with the help of the treating physicians. Surviving recipients were recalled by their treating physicians for an office visit, at which time an examination for evidence of liver disease was carried out and blood was drawn for measurement of liver function tests. Liver disease was defined as an elevation in the serum alanine aminotransferase greater than 2.5 times the upper limit of normal on two or more occasions at least 2 wk apart. Liver disease was characterized as acute and chronic, respectively, if the duration of alanine aminotransferase elevation was less than or greater than 6 mo. The cause of liver disease was assigned from the clinical, serological, and histopathological data available in the hospital records. Because records were reviewed without knowledge of pretransplantation anti-HCV or GBV-C RNA, liver disease consistent with acute or chronic viral hepatitis, but not due to any other cause, was classified as non-A, non-B hepatitis (NANBH).

RT-PCR for GBV-C RNA

Sera were tested for GBV-C genomic RNA by RT-PCR at Abbott Laboratories (North Chicago, IL). RNA was isolated from 25 µl of human sera using a commercially available kit (Qiagen, Inc., Chatsworth, CA), according to the manufacturer’s instructions. The extracted RNA (7.5%) was converted to cDNA in the presence of random hexamers, using a commercially available kit as directed by the manufacturer (Perkin-Elmer, Foster City, CA). One-fifth of the resulting cDNA product was used in each of two separate PCR reactions (25 µl), using degenerate primers derived from the NS3 helicase region of GBV-C, as described previously (21), or using primers derived from the GBV-C 5' untranslated region (UTR) (ntrC-S1:5'-CACTGGGTGCAACGCCCCAGAA-3' and ntrC-A1:5'-CACTGGTCTTGTCAACTCGC-3') (22). The final concentration of 5'-UTR primers was 0.5 µM. Thermocycling conditions for 5'-UTR primers used 40 cycles of denaturation-annealing-extension (94°C, 20 s; 55°C, 30 s; 72°C, 45 s) followed by a 10-min extension at 72°C. Completed reactions were held at 4°C. PCR products were separated by agarose gel electrophoresis, transferred to Hybond-N nylon filters (Amersham, Inc., Arlington Heights, IL), and hybridized under low stringency to a radiolabeled probe consisting of a cDNA fragment from the NS3 region (10) or from the 5' end of the GBV-C genome (nucleotides 13 to 631) (12). Samples were considered GBV-C-positive only if hybridizable PCR products of the appropriate size were detected using both sets of primers.

Statistical Analyses

Pearson’s statistic for the chi-square test or Fisher’s test (when appropriate) was used for comparisons of discrete variables between patients with and without pretransplantation GBV-C RNA. Results are expressed as fraction-positive (percentage). For continuous variables, the statistical significance of the differences between the two groups was assessed by the Wilcoxon two-sample test. Results are expressed as median (interquartile range). The Mantel-Haenszel test was used when the outcome was ordinal. A Cox proportional hazards model was used to calculate the relative risk (RR) and 95% confidence interval (CI) of the RR for patients with pretransplantation GBV-C RNA compared with patients without pretransplantation GBV-C RNA. The RR were calculated for posttransplantation liver disease, posttransplantation NANBH, graft loss, death, and death due to sepsis, with and without adjustment for anti-HCV. Tied survival times were adjusted by the Breslow method. Differences between groups were considered significant if the P value was <0.05 and as a nonsignificant trend if P was between 0.05 and 0.1. Analyses were run in Statistical Analysis System/Stat Version 6.10 (Statistical Analysis System Institute Inc., Cary, NC) and Splus 3 for Windows, version 3.3 (Statistical Services Inc., Seattle, WA).

Results

Prevalence of GBV-C RNA

Pretransplantation GBV-C RNA was present in 18 of 99 (18%, 95% CI, 17.2 to 18.8%) recipients in whom sera were available for testing. The prevalence of GBV-C RNA was not significantly different (P = 0.70) from the prevalence of anti-HCV (22 of 99, 22%) in the same population. GBV-C RNA was present in 5 of 22 (23%) anti-HCV-positive recipients compared with 13 of 77 (17%) anti-HCV-negative recipients (P = 0.53). GBV-C RNA was present in 2 of 17 (12%) HCV RNA (detected by PCR)-positive patients compared with 16 of 81 (20%) HCV RNA-negative patients (P = 0.44). These results suggest that the prevalence of GBV-C RNA was not increased among recipients with serum markers of HCV infection compared with recipients without serum markers of HCV.

Pretransplantation Characteristics of Recipients with and without Pretransplantation GBV-C RNA

As shown in Table 1, the median number of pretransplantation blood transfusions among recipients with GBV-C RNA
was significantly higher than among GBV-C-negative recipients \((P = 0.05)\). In addition, there was a trend toward longer duration since initiation of dialysis in GBV-C-positive patients compared with GBV-C RNA-negative patients \((P = 0.09)\). History of liver disease, markers of hepatitis B virus (HBV), HCV, and cytomegalovirus infections were not significantly different between the two groups.

**Posttransplantation Characteristics and Outcomes of Recipients with and without Pretransplantation GBV-C RNA**

As shown in Table 2, duration of follow-up (until December 1993), number of rejections, prevalence, cause, and type of posttransplantation liver disease were not significantly different between the groups. Posttransplantation sera were available for GBV-C RNA testing in 63 recipients. Interestingly, 5 of 10 (50%) patients with pretransplantation GBV-C RNA tested negative after transplantation, and 8 of 53 (15%) patients without pretransplantation GBV-C RNA tested positive after transplantation. Donor sera from five of the eight patients in the latter group were available, and only one of them (20%) tested positive for GBV-C RNA.

Information on graft and patient survival was updated until December 1995. As shown in Table 3, duration of follow-up, graft, and patient survival were not significantly different between groups. Causes of graft loss (available in 33 of 36 patients who lost their grafts) and death were also not significantly different between the groups. The RR of posttransplantation liver disease, posttransplantation NANBH, graft loss, death, and death due to sepsis, and the survival curves are shown in Table 4 and Figures 1 through 4, respectively. Although the RR for posttransplantation liver disease and posttransplantation NANBH were increased for patients with pretransplantation GBV-C infection, the CI were wide, and hence not statistically significant. The RR for graft loss and death were not increased. When adjusted for pretransplantation anti-HCV, the RR for posttransplantation liver disease, posttransplantation NANBH, graft loss, and death did not change appreciably.

**Discussion**

Patients on chronic dialysis are at increased risk of acquiring parenterally transmitted hepatitis viruses from blood product transfusions or nosocomial transmission in hemodialysis units (23–27). Indeed, among dialysis patients, serum markers of HBV and HCV have been reported in 0.3 to 25.9% and 3.3 to 55%, respectively (28–35). The clinical consequences of these infections are especially manifest after renal transplantation, and patients with pretransplantation HBV or HCV infection are at increased risk of posttransplantation liver disease and death (20,36). The discovery of yet another parenterally transmitted hepatitis virus, GBV-C, raises questions about the prevalence and risk factors for this infection among patients undergoing renal transplantation and its impact on posttransplantation clinical outcomes.

The 18% prevalence of GBV-C among dialysis patients...
Table 2. Posttransplantation characteristics of kidney transplant recipients with and without GBV-C RNA before transplantation

<table>
<thead>
<tr>
<th>Posttransplantation Characteristics</th>
<th>GBV-C RNA-Positive (n = 18)</th>
<th>GBV-C RNA-Negative (n = 81)</th>
<th>P value&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow-up (months)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>64 (27 to 82)</td>
<td>56 (3 to 78)</td>
<td>0.48</td>
</tr>
<tr>
<td>Number of rejections</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>7 of 18 (39%)</td>
<td>31 of 81 (38%)</td>
<td>0.38</td>
</tr>
<tr>
<td>1</td>
<td>10 of 18 (56%)</td>
<td>30 of 81 (37%)</td>
<td></td>
</tr>
<tr>
<td>≥2</td>
<td>1 of 18 (5%)</td>
<td>20 of 81 (25%)</td>
<td></td>
</tr>
<tr>
<td>Courses of antilymphocyte antibodies</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>9 of 18 (50%)</td>
<td>41 of 81 (51%)</td>
<td>0.48</td>
</tr>
<tr>
<td>1</td>
<td>6 of 18 (33%)</td>
<td>27 of 81 (33%)</td>
<td></td>
</tr>
<tr>
<td>≥2</td>
<td>3 of 18 (17%)</td>
<td>13 of 81 (16%)</td>
<td></td>
</tr>
<tr>
<td>Liver disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of rejections</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>6 of 17 (35%)</td>
<td>22 of 80 (28%)</td>
<td>0.52</td>
</tr>
<tr>
<td>Cause of liver disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NANBH</td>
<td>3 of 17 (18%)</td>
<td>8 of 80 (10%)</td>
<td>0.63</td>
</tr>
<tr>
<td>others</td>
<td>3 of 17 (18%)</td>
<td>14 of 80 (18%)</td>
<td>0.74</td>
</tr>
<tr>
<td>Type of liver disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>acute</td>
<td>3 of 6 (50%)</td>
<td>12 of 22 (55%)</td>
<td>0.84</td>
</tr>
<tr>
<td>chronic</td>
<td>3 of 6 (50%)</td>
<td>10 of 22 (45%)</td>
<td></td>
</tr>
<tr>
<td>Anti-HCV (ELISA2)-positive</td>
<td>1 of 11 (9%)</td>
<td>11 of 54 (20%)</td>
<td>0.38</td>
</tr>
<tr>
<td>HCV RNA (PCR)-positive</td>
<td>2 of 11 (18%)</td>
<td>10 of 53 (19%)</td>
<td>0.96</td>
</tr>
<tr>
<td>GBV-C RNA (PCR)-positive</td>
<td>5 of 10 (50%)</td>
<td>8 of 53 (15%)</td>
<td>0.01</td>
</tr>
</tbody>
</table>
| a Data for continuous variables are presented as median (interquartile range) and for discrete/ordinal variables as fraction-positive (percentage). NANBH, non-A, non-B hepatitis. Other abbreviations as in Table 1.
| b Chi-square/Fisher's tests were used for discrete variables, Wilcoxon test for continuous variables, and Mantel-Haenszel test for ordinal outcomes.
| c Until December 1993.

Table 3. Posttransplantation outcomes of kidney transplant recipients with and without GBV-C RNA before transplantation

<table>
<thead>
<tr>
<th>Posttransplantation Outcome</th>
<th>GBV-C RNA-Positive (n = 18)</th>
<th>GBV-C RNA-Negative (n = 81)</th>
<th>P value&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow-up (months)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>89 (70 to 98)</td>
<td>77 (61 to 95)</td>
<td>0.34</td>
</tr>
<tr>
<td>Graft loss</td>
<td>7 of 17 (41%)</td>
<td>36 of 80 (45%)</td>
<td>0.77</td>
</tr>
<tr>
<td>Cause of graft loss</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>acute rejection</td>
<td>3 of 7 (43%)</td>
<td>14 of 33 (42%)</td>
<td>0.44</td>
</tr>
<tr>
<td>chronic rejection</td>
<td>1 of 7 (14%)</td>
<td>11 of 33 (33%)</td>
<td></td>
</tr>
<tr>
<td>death</td>
<td>3 of 7 (43%)</td>
<td>6 of 33 (18%)</td>
<td></td>
</tr>
<tr>
<td>others</td>
<td>0 of 7 (0%)</td>
<td>2 of 33 (6%)</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>4 of 17 (24%)</td>
<td>19 of 79 (24%)</td>
<td>0.96</td>
</tr>
<tr>
<td>Cause of death</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>sepsis</td>
<td>2 of 4 (50%)</td>
<td>9 of 19 (47%)</td>
<td>0.97</td>
</tr>
<tr>
<td>liver failure</td>
<td>0 of 4 (0%)</td>
<td>1 of 19 (5%)</td>
<td></td>
</tr>
<tr>
<td>others</td>
<td>1 of 4 (25%)</td>
<td>5 of 19 (26%)</td>
<td></td>
</tr>
<tr>
<td>unknown</td>
<td>1 of 4 (25%)</td>
<td>4 of 19 (21%)</td>
<td></td>
</tr>
<tr>
<td>Death due to liver failure/sepsis</td>
<td>2 of 17 (12%)</td>
<td>10 of 79 (13%)</td>
<td>0.92</td>
</tr>
</tbody>
</table>
| a Data for continuous variables are presented as median (interquartile range) and for discrete variables as fraction-positive (percentage). Abbreviations as in Table 1.
| b Chi-square/Fisher's tests were used for discrete variables, Wilcoxon test for continuous variables.
| c Until December 1995.

undergoing renal transplantation in our study is in sharp contrast to the 3.1% prevalence among chronic hemodialysis patients in Japan, reported by Masuko and colleagues (17), and the 55% prevalence among chronic hemodialysis patients in Indonesia, reported by Tsuda and colleagues (18). The higher prevalence of GBV-C infection among patients in our study compared with those reported by Masuko and colleagues is particularly surprising because the patients in the latter study...
Table 4. Relative risks of adverse posttransplantation outcomes among kidney transplant recipients with pretransplantation GBV-C RNA compared with recipients without pretransplantation GBV-C RNA

<table>
<thead>
<tr>
<th>Post-Transplantation Outcome</th>
<th>Risk Ratio (95% CI)* Unadjusted for Anti-HCV Status</th>
<th>P valueb</th>
<th>Risk Ratio (95% CI)* Adjusted for Anti-HCV Status</th>
<th>P valueb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver disease</td>
<td>1.37 (0.55 to 3.40)</td>
<td>0.50</td>
<td>1.18 (0.48 to 2.94)</td>
<td>0.72</td>
</tr>
<tr>
<td>NANBH</td>
<td>2.09 (0.64 to 6.79)</td>
<td>0.22</td>
<td>1.84 (0.56 to 6.02)</td>
<td>0.31</td>
</tr>
<tr>
<td>Graft loss</td>
<td>0.88 (0.37 to 2.09)</td>
<td>0.77</td>
<td>0.88 (0.37 to 2.10)</td>
<td>0.78</td>
</tr>
<tr>
<td>Death</td>
<td>0.92 (0.31 to 2.72)</td>
<td>0.88</td>
<td>0.89 (0.30 to 2.62)</td>
<td>0.83</td>
</tr>
<tr>
<td>Death due to sepsis or liver failure</td>
<td>1.00 (0.22 to 4.64)</td>
<td>0.99</td>
<td>0.93 (0.20 to 4.32)</td>
<td>0.93</td>
</tr>
</tbody>
</table>

* 95% confidence limits of the risk ratio. CI, confidence interval. Other abbreviations as in Tables 1 and 2.

b Cox proportional hazards model, P value by Wald chi-square test.

had been on dialysis much longer (mean, >7 yr) than patients in our study (mean, <3 yr). There are several possible explanations for the differences in prevalence between these two studies. First, the 0.9% prevalence of GBV-C infection among volunteer blood donors in Japan (17) is lower than the 1.7% prevalence among the volunteer blood donors in the United States (13). Consequently, Japanese dialysis patients may be at a lower risk of acquiring GBV-C infection from blood product
transfusions than their U.S. counterparts. Second, the primers used by Masuko and colleagues for the detection of virus may have been less sensitive, thus underestimating the prevalence. Third, there may be geographic differences in the prevalence of GBV-C due to differences in host susceptibility or virulence of different strains of GBV-C. In contrast, the higher prevalence of GBV-C infection among chronic hemodialysis patients in Indonesia is not surprising because the prevalence of anti-HCV was also extremely high (79%), probably reflecting suboptimal infection control strategies in those dialysis units.

Among patients undergoing renal transplantation in this study, patients with GBV-C infection received a higher number of blood transfusions and exhibited a trend toward a longer duration of dialysis compared with patients without GBV-C infection. These are both known risk factors for parenterally transmitted viral infections among dialysis patients (23,37–40) and, hence, offer additional evidence that GBV-C infection is transmitted by parenteral routes. Interestingly, the 23% prevalence of GBV-C infection among anti-HCV-positive patients was not significantly different from the 17% prevalence among anti-HCV-negative patients. Likewise, Tsuda and colleagues have also reported no significant difference in the prevalence of GBV-C RNA among hemodialysis patients with anti-HCV (57%) and without anti-HCV (50%) (18). These data suggest that GBV-C infection in dialysis patients may be acquired independently and from different sources. In contrast, among cadaver organ donors, GBV-C RNA was present in a significantly higher proportion of anti-HCV-positive donors compared with anti-HCV-negative donors (28% versus 7%, $P = 0.001$) (15). Further, HCV (41) and GBV-C (15) infection among cadaver organ donors are associated with high-risk social behavior. These data suggest that HCV and GBV-C are probably acquired concurrently from the same source in cadaver organ donors, but not in dialysis patients.

We observed that 5 of 10 (50%) patients with pretransplantation GBV-C infection tested negative for GBV-C RNA post-
transplantation, suggesting that some patients do clear the virus despite immunosuppression. This is in contrast to HCV infection, which appears to persist indefinitely in both immunosuppressed and nonimmunosuppressed patients (42–45). Interestingly, 8 of 53 (15%) patients without pretransplantation GBV-C infection tested positive after transplantation. Among five patients in this group in whom donor sera were available for GBV-C RNA testing, only one donor (20%) was positive for GBV-C infection. Others may have acquired the infection from perioperative blood transfusions or other sources during the interval between transplantation and collection of the posttransplantation serum specimen.

We observed no statistically significant difference in the prevalence of posttransplantation liver disease in general, or NANBH in particular, between patients with and without pretransplantation GBV-C infection. However, the observed risks were higher (1.37 for posttransplantation liver disease and 2.09 for NANBH) in patients with pretransplantation GBV-C infection, but the CI were wide (0.55 to 3.40 and 0.64 to 6.79, respectively). Thus, we cannot definitely exclude a role for GBV-C in posttransplantation liver disease. It is also possible that a longer follow-up may be required to show an association of pretransplantation GBV-C infection with posttransplantation liver disease. If there is an effect of pretransplantation GBV-C infection on posttransplantation liver disease, it is much less than the effect of pretransplantation HCV infection. Indeed, in the same cohort of patients, patients with pretransplantation anti-HCV had a fivefold higher risk of posttransplantation liver disease compared with patients without pretransplantation anti-HCV (20). The role of GBV-C in posttransplantation liver disease needs to be examined further in a larger population.

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Figure 3. Kaplan-Meier estimate of graft survival among recipients with GBV-C RNA (—) and without GBV-C RNA (—–) before transplantation. Death with a functioning graft was included as a cause of graft loss. The RR of graft loss among recipients with pretransplantation GBV-C RNA (and 95% CI of the risk) was calculated using a proportional hazards model. The number of patients at risk at the beginning of each 12-mo interval is provided for recipients with pretransplantation GBV-C RNA (lower series) and recipients without pretransplantation GBV-C RNA (upper series).
Relative Risk: 0.92 (0.31, 2.72)

Figure 4. Kaplan-Meier estimate of patient survival among recipients with GBV-C RNA (-----) and without GBV-C RNA (-----) before transplantation. The RR of death among recipients with pretransplantation GBV-C RNA (and 95% CI of the risk) was calculated using a proportional hazards model. The number of patients at risk at the beginning of each 12-mo interval is provided for recipients with pretransplantation GBV-C RNA (lower series) and recipients without pretransplantation GBV-C RNA (upper series).

GBV-C Negative:
- Time (Months): 12 24 36 48 60 72 84 96 108
  - Patients: 79, 72, 71, 69, 65, 61, 47, 34, 20, 0

GBV-C Positive:
- Time (Months): 12 24 36 48 60 72 84 96 108
  - Patients: 17, 16, 15, 15, 15, 14, 12, 11, 6, 0

Organ Bank. Participants include the New England Organ Bank, Newton, MA (Robert L. Kirkman, Brian J. G. Pereira, Andrew S. Levey); Yale-New Haven Hospital, New Haven, CT (Marc I. Lorber); Maine Medical Center, Portland, ME (Donald A. Leeber); Beth Israel Hospital (Michael E. Shapiro); Brigham and Women’s Hospital (Edgar L. Milford, Dianne B. McKay); Children’s Hospital Medical Center (William E. Harman); Massachusetts General Hospital (Jules L. Dienstag); New England Deaconess Hospital (Anthony P. Monaco, W. David Lewis, David Shaffer); New England Medical Center (Beth A. Bouthot, Svetlozar N. Natov, B. V. R. Murthy, Christopher H. Schmid, Richard B. Freeman); Veteran’s Administration Medical Center, University Hospital, Boston, MA; Lahey Clinic Medical Center, Burlington, MA (Samir D. Kassissieh); Baystate Medical Center, Springfield, MA (George A. Lipkowitz); University of Massachusetts Medical Center, Worcester, MA (Raja B. Khuali); State Laboratory Institute, Jamaica Plain, MA (Barbara G. Werner); and Medical Center Hospital of Vermont, Burlington, VT (Virginia L. Hood).

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