

# Renal Transplantation Issues in HCV Infected Donors and Recipients

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HCV is the most common chronic blood-borne infection in the United States. Its prevalence is currently estimated at no less than 1.8% and is projected to increase four times from 1990 to 2015. HCV transmission by organ and tissues transplantation has been unequivocally demonstrated. Therefore, the overwhelming majority of organ procurement organizations (OPOs) presently screen organ donors for HCV infection. Serologic tests that detect antibodies to HCV (anti-HCV) are the mainstay of the diagnosis of HCV infection. However, these tests cannot differentiate between viremic and non-viremic anti-HCV positive organ donors and consequently cannot determine donor infectivity. Further testing for HCV RNA by PCR or bDNA is required to allow assessment of the risk of transmitting HCV from the donor to the recipients. In the case of cadaver organ donors, this is precluded by the time constraint of the organ preservation period. Recently developed assays for HCV core antigen (HCVcAg) seem to be a viable alternative to HCV RNA testing. These assays can detect HCV infection prior to anti-HCV seroconversion and have demonstrated excellent correlation with tests for HCV RNA.

The rate of transmission of HCV infection by anti-HCV-positive donors at different centers varies widely. Among recipients of organs from anti-HCV- positive donors, 35% (range 0-55%) develop post-transplant liver disease, 50% (range 14-100%) test positive for anti-HCV after transplantation, and 73% (range 14-96%) test positive for HCV RNA by PCR. These variations could be due to the following reasons: 1) In the absence of HCV RNA testing, clinical or laboratory evidence of liver disease and testing for anti-HCV alone among organ transplant recipients may significantly underestimate the prevalence and transmission of HCV infection. 2) Since the risk of HCV transmission by organ and tissue transplantation could be related to the prevalence of HCV RNA among anti-HCV-positive donors, a lower prevalence of HCV RNA among anti-HCV-positive cadaver donors at some centers could explain the lower rate of HCV transmission by organs procured from these donors. 3) The renal preservation method, static vs perfusion storage, could account for differences in the amount of the viral inoculum transmitted by anti-HCV positive kidneys.

The prevalence of HCV infection among cadaver organ donors varies world- wide between 1.08 and 11.8%. In the U.S., the prevalence of anti-HCV by ELISA I is 5.1%, the extrapolated prevalence of anti-HCV by ELISA 2 - 4.2% and that of HCV RNA - 2.4%. The prevalence of anti-HCV among cadaver organ donors is several-fold higher than the prevalence of anti-HCV among healthy blood donors, probably due to the higher prevalence of risk factors, among cadaver organ donors, associated with the spread of viral infections, such as unsuspected intravenous drug use or sexual promiscuity.

The use of kidneys from anti-HCV positive donors has been associated with a higher risk of liver disease in the post-transplant period, but has shown no significant adverse effect on patient or graft survival. Different transplant policies have been developed to prevent HCV transmission by organ and tissue trans- plantation but at the same time to avoid unnecessary discarding of donors. A policy of screening organ donors with ELISA 2 and using organs only from anti-HCV-negative donors carries negligible or no risk of transmitting HCV because ELISA 2 has a test sensitivity of 100% and a negative predictive value of 100%. A policy of restricting the use of organs from anti-HCV-positive donors to life-saving transplants (heart, liver or lung) has been adopted by the majority of OPOs worldwide. Because not all anti-HCV positive donors are infectious, discarding all anti-HCV positive kidneys would lead to undesirable waste of organs. Consequently, this practice has been challenged and consideration has been given to the use of such kidneys under certain circumstances.

To minimize the waste of anti-HCV-positive kidneys, some transplant centers have adopted a policy of transplanting kidneys from anti-HCV-positive donors into anti-HCV-positive recipients. Such practice would eliminate the waste of anti-HCV-positive kidneys and has not demonstrated any adverse effect on patient survival. A better alternative seems to be a policy of transplanting kidneys from anti-HCV-positive donors only in HCV RNA-positive recipients. However, this requires HCV RNA testing of all anti-HCV-positive dialysis patients awaiting renal transplantation. Although transplantation of kidneys

from anti-HCV-positive donors into anti-HCV-positive recipients appears to be safe, this strategy should be considered an experimental treatment until more data become available.

The prevalence of pre-transplantation anti-HCV among renal transplant recipients is 11 to 49%. Pre-transplantation anti-HCV is associated with an increased prevalence of post-transplant liver disease, 19 to 64% among anti-HCV positive recipients vs. 1 to 30% among anti-HCV negative recipients. Although pre-transplantation anti-HCV is found consistently to be associated with an increased risk of post-transplantation liver disease, post-transplantation patient survival was adversely affected in only some studies.

The effect of renal transplantation on the course of HCV infection in dialysis patients has been a subject of controversies. A study of dialysis patients referred for renal transplantation to the transplant centers served by the New England Organ Bank has demonstrated that, among the anti-HCV positive renal transplant candidates, patients who received a transplant had an initially higher risk of death (4.75 between 0 to 3 months and 1.76 between 4 to 6 months), but a lower risk thereafter (0.31 between 7 months and 4 years, and 0.84 after 4 years) than those who remained on dialysis. This pattern was not affected by the HCV genotype or type of HCV infection. These findings suggest that renal transplantation has a beneficial rather than adverse effect on long-term survival in anti-HCV positive patients. Therefore, anti-HCV positive status alone in renal transplant candidates should not be considered a contraindication for renal transplantation.