

HCV Related Kidney Disease after Kidney Transplantation

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Since the introduction of serologic testing for HCV in the early 1990's, there has been a significant interest in the outcomes of transplant recipients receiving hepatitis C positive kidneys or who were hepatitis C positive at the time of transplantation. The initial focus was on patient and graft survival. The consensus in the transplant community at this time is that transplantation of HCV positive recipients, even with HCV positive donors does not confer an increased risk of graft loss or death following transplantation. Transplantation of HCV positive donors into HCV negative recipients is more controversial. There is no question that these transplants confer a greater risk of patient mortality and graft loss in some patients. Thus, most of these transplants are only performed in special circumstances where the risk of dialysis mortality may be greater than receiving a HCV positive kidney or in dialysis recipients who have no vascular access.

HCV related kidney disease was first described in the early 1990's and was associated with the discovery of kidney disease associated with the production of mixed cryoglobulins that may cause kidney injury. Membranoproliferative glomerulonephritis (MPGN) is the commonly reported glomerulopathy caused by HCV infection. Membranous nephropathy is the next most common glomerulopathy associated with chronic HCV infection.

Since these reports of glomerulopathy in native kidneys, there have been numerous reports of both MPGN and membranous nephropathy occurring in kidney transplant recipients with HCV infection. The role of cryoglobulins in the pathogenesis of the kidney disease in transplant recipients is less clear. Other reported diseases in transplant recipients include acute transplant glomerulopathy (a form of acute rejection) and acute thrombotic microangiopathy (TMA). Recently, an association of chronic allograft nephropathy (CAN) has been described in HCV infected recipients.

The development of CAN in kidney transplant recipients is manifested clinically by an increasing serum creatinine with proteinuria. Recently, two reports demonstrated a higher incidence of proteinuria in HCV positive transplant recipients. In both series, the underlying etiology for the kidney dysfunction was more likely to be CAN, although MPGN and membranous nephropathy were found on some biopsies. In both of these series, the incidence of recurrent or de novo nephropathy was not different from recipients who were HCV negative. These data suggest that HCV positive transplant recipients have a higher risk of late graft loss due to CAN.

We examined the outcomes of HCV positive recipients receiving an HCV positive or negative kidney, HCV negative recipients receiving an HCV positive kidney and patients without HCV infection receiving a cadaver transplant at our center since 1990. The numbers of patients in each category is shown below:

D-/R-	D-/R+	D+/R-	D+/R+	Total
1139 (83%)	43 (3%)	115 (9%)	71 (5%)	1368

There were significant demographic differences in the four groups. Criteria developed for HCV + donors into HCV- recipients included patients with a high risk for death on dialysis. These patients were older (average age 55 yrs) and 50% were diabetics ($p=0.001$). More retransplants were performed in the D-/R+ and D+/R+ groups ($p=0.001$). Blacks accounted for 21% of the D-/R+ and 45% of the D+/R+ groups compared to 8% of D-/R- and 6% of D+/R- groups ($p=0.001$). More HCV kidneys were transplanted before 1996 ($p=0.001$). Because of the differences in the groups, the analysis was adjusted for these covariates.

Graft survival and patient survival were poorer in all of the groups with HCV infection prior to transplant or receiving a HCV positive kidney transplant ($p=0.001$). The 10 year survivals are shown below:

	D-/R-	D-/R+	D+/R-	D+/R+
Graft Survival	50%	15%	23%	29%
Patient Survival	72%	55%	50%	51%

There were no statistical differences in infection or acute rejection between the four groups. There was a significant difference in the incidence of CAN between the groups ($p=0.001$). At 10 years, there was a 23% incidence of CAN in the D-/R- group. This compared to an incidence of 41% in the D-/R+, 44% in the *D+TR-*, and 43% in the D+/R+ groups.

It would appear from this data that there is a significant risk for graft loss in the late transplant period due to CAN. There may also be a significant mortality risk in patients with HCV infection or in recipients who are HCV negative and receive a HCV positive kidney transplant.