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Clinical Nephrology 2019: Transplanting kidneys from CMV-seropositive donors to CMV-seronegative recipients is not associated with poorer renal allograft function or survival

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Background: Cytomegalovirus (CMV)-seronegative recipients of renal allografts from CMV-seropositive donors (D+/R−) have a higher rate of acute rejection than other renal transplant recipients. A relationship between CMV infection/disease and chronic allograft nephropathy (CAN) has been proposed from animal studies, although human studies have been inconclusive. The objective of this study was to determine if CMV seromatching has an effect on renal allograft function and allograft survival.

Methods: A retrospective single centre study was carried out in 333 first cadaveric transplant recipients from January 1, 1991 to December 31, 1997. The primary end-point was creatinine clearance at 3 years post-transplant in groups based on CMV seromatching. The secondary end-point was renal allograft survival.

Results: Mean creatinine clearance 3 years post-transplant was 53.4 ml/min/1.73 m2 of body surface area. There was no significant difference in the mean creatinine clearance for groups formed on the basis of CMV seromatching. Delayed graft function and acute rejection were associated with a lower creatinine clearance at 3 years and reduced overall graft survival [hazard ratios 2.35 (1.56–3.54) (P<0.001) and 1.57 (1.0–2.46) (P = 0.046), respectively]. Considering the end-point of graft loss due to acute rejection (censoring for death with a functioning graft) identified the D+/R− group as having an increased hazard of graft loss due to acute rejection [hazard ratio 3.12 (1.16–8.57) (P = 0.024)].

Conclusions. The D+/R− group does not appear to have poorer renal allograft function 3 years post-transplant. This group does, however, have an increased risk of early allograft loss due to acute rejection.

Introduction: Cytomegalovirus (CMV) disease incurs significant morbidity and health care costs in the setting of organ transplantation [1]. The risk of CMV infection and CMV disease following transplantation is highest in CMV-seronegative recipients of renal allografts from CMV-seropositive donors (D+/R−), i.e. recipients who have no immunity to the virus and receive a kidney from a donor who has been infected previously [2]. In addition to the direct effects of viral infection, there is also evidence of an association between CMV infection/disease and acute allograft rejection in the setting of renal and other solid organ transplantation [3–5]. The nature of this relationship is a matter of debate, with evidence supporting both a 'forward' relationship (CMV infection/disease precedes acute rejection) and a 'backward' relationship (CMV infection/disease follows acute rejection) [6]. We recently demonstrated that seromismatched recipients of renal allografts had a significantly higher rate of acute rejection than non-seromismatched recipients, supporting a forward relationship [7]. A relationship between CMV infection/disease and chronic allograft nephropathy (CAN) has been proposed, and several animal studies have demonstrated mechanisms by which CMV infection/disease may enhance the process of chronic allograft nephropathy [8–10]. It is unclear, however, if this effect is independent of the effects of acute rejection on the development of CAN.

The objective of this study was to determine if CMV matching has an effect on renal allograft function and allograft survival that is independent of its effect of acute rejection.

Note: The work is Submitted from International Conference on Kidney Disease and Disadvantages March 2015, Spain Italy

Results: Three hundred and thirty-three patients (216 males) underwent first cadaveric renal transplant during this time period. Mean age (±SD) at the time of transplantation was 46.6 years (±12.6). Mean cold ischaemic time was 24.7 h (±7.9). Fifty patients (15%) received a biological induction agent and 111 patients (33%) had delayed graft function. One hundred and ninety-four (58.3%) patients had at least one acute rejection episode. Mean creatinine clearance 3 years post-transplant was 53.4 ml/min/1.73 m2 body surface area (BSA). Graft survival [±95% confidence interval (CI)] 3 years post-transplant was 78% (72.7–82.0). Table 1 shows the variables affecting the creatinine clearance at 3 years by simple linear regression. In this table, the groups formed on the basis of donor and recipient CMV serostatus are: donor negative/recipient positive (D−/R+); donor positive/recipient negative (D+/R−); donor positive/recipient positive (D+/R+); and donor negative/recipient negative (D−/R−). In the models, the four CMV groups were considered as three 'dummy' variables with the D−/R− group as the control and one dummy variable representing each of the other three groups. Despite not reaching the required level of significance by univariate analysis, CMV serostatus was entered into the multiple linear regression model as this was the primary variable under study. All interaction terms were non-significant. The final model contained three variables of which two, delayed graft function and acute rejection, had an independent and significant effect on the square root of creatinine clearance at 3 years. Compared with those who had no delayed graft function, individuals who experienced delayed graft function had a reduction in creatinine clearance at 3 years of −5.42 ml/min/1.73 m2 BSA. Compared with those who had no acute rejection, individuals who experienced acute rejection had a reduction in creatinine clearance at 3 years of −5.39 ml/min/1.73 m2 BSA. These data are shown in Table 2. The use of biological induction remained in the final model although the effect failed to reach the level of statistical significance.

Discussion: The primary objective of this study was to determine if CMV seromatching has an effect on renal allograft function that is independent of its effect of acute rejection. In the absence of histological data (protocol biopsies were not performed during this time period), creatinine clearance was used as a marker of allograft function and as a surrogate for CAN [13]. The results observed here suggest that CMV-seronegative recipients of renal allografts from CMV-seropositive donors do not have poorer renal allograft function 3 years post-transplant. This result should, however, not be considered in isolation as the creatinine clearance measurements reflect only values from patients who had functioning grafts at 3 years. The importance of this is underscored by the fact that the D+/R− group have an increased risk of allograft loss due to acute rejection. Overall, the results of our previous and present studies on the effects of CMV seromismatching would suggest that the D+/R− group has an increased risk of acute renal allograft rejection and early graft loss due to acute rejection. If, however, the allograft is not lost due to acute rejection, the allograft function appears to be similar to that of other groups as judged by either creatinine clearance or graft survival (note that the survival curves in Figure 2 are parallel after the initial post-transplant period).

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