

Posttransplant Infections Following Pretransplant Immunosuppression for Glomerulonephritis

By Grant Kirby, Robin K. Avery, and Divyanshu Malhotra

Temporal trends in the diagnosis of glomerulonephritis (GN) suggest an overall increase in incident cases over the past decades, with immunosuppression being the mainstay therapeutic approach for many of these conditions (1, 2). Despite advances in treatment, the estimated proportion of kidney failure in the United States attributable to GN remains high, with an increased need for kidney transplantation (3, 4). Various posttransplant endpoints have been studied in this and other patient populations: rates of recurrent GN, graft failure, survival, or quantifying infection risk based on degrees of immunosuppression (5, 6). Infrequently considered is the effect of the pretransplant period in individuals with GN on posttransplant outcomes. The recent article, “Infections Following Kidney Transplantation After Exposure to Immunosuppression for Treatment of Glomerulonephritis” (7), puts forward an important question in bridging this connection: Do individuals receiving pretransplant immunosuppression (PTI) in the management of GN have different rates of posttransplant infectious complications?

Massicotte-Azarniouch et al. (7) conducted a single-center retrospective cohort study, using clinical data over a 15-year period on kidney transplant recipients who were nondiabetic, to compare the rate of developing their first BK virus (BKV), cytomegalovirus (CMV), or bacterial infection in the posttransplant period between individuals receiving PTI for the treatment of GN and those who did not. PTI included a cumulative dose history of cyclophosphamide and rituximab and duration of exposure to high-dose steroids (defined as ≥ 20 mg of prednisone for ≥ 4 weeks), mycophenolate, azathioprine, and calcineurin inhibitors. Additional details included in the analysis were donor-recipient status for CMV and Epstein-Barr virus, use and type of T cell depletion for induction, and maintenance therapy prescribed at

time of transplantation. The authors' primary finding demonstrated no significant difference in the hazard ratio of developing either viral (BKV or CMV) or bacterial infection posttransplantation between the two groups. Interestingly, there were decreased rates of viral infection in the PTI group after adjusting for demographics, dialysis vintage, type of transplant, and induction/maintenance therapies.

While convincing, we feel these results would be further reinforced with additional details regarding the cumulative dose of T cell depletion therapy (thymoglobulin) and its response, BKV and CMV monitoring protocols, inclusion of viral infections other than BKV and CMV, fungal infections, and longitudinal information on maintenance immunosuppression and prophylaxis. The significant differences in age, gender, and dialysis vintage also raise concern for possible residual confounding, which might contribute to the observed difference in viral infection and trend toward a higher rejection rate in the PTI group (although not significant). Finally, there is increasing recognition of the cumulative morbidity of recurrent infections (6), which is not fully reflected in analyses based on the first occurrence of an infection.

Despite these concerns, this study benefits from its large population size, years of longitudinal follow-up, detailed pretransplant and posttransplant clinical history, inclusion of cumulative drug exposure pretransplant, and thoughtful statistical analysis. These findings, along with conceptual frameworks like the “net state of immunosuppression” (8), contribute to our ability to discern which individuals may be at higher risk for posttransplant infections, which remain a significant source of both morbidity and mortality (6, 9). This research will help to add nuance to clinical practice in the field. ■

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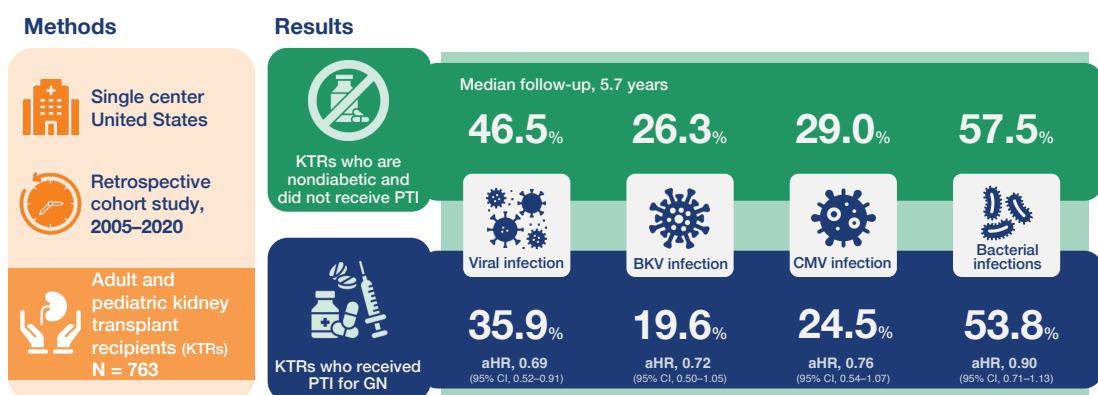
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Is there an increased risk of infection following kidney transplantation in those who received pretransplant immunosuppression for the treatment of glomerulonephritis?

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Conclusions: Use of PTI for the treatment of GN was not associated with an increased risk of viral or bacterial infection after transplantation.

Massicotte-Azarniouch D, et al. Infections Following Kidney Transplantation After Exposure to Immunosuppression for Treatment of Glomerulonephritis. *Am J Kidney Dis* (published online December 30, 2023). doi: 10.1053/ajkd.2023.10.016

aHR, adjusted hazard ratio; CI, confidence interval.

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