# BK Nephropathy in Kidney Transplantation

A recently published Cochrane systematic review by Wajih et. al., examined the current clinical approaches to addressing BK virus-associated nephropathy (BKVAN) in kidney transplant recipients. BK virus reactivation is common among this population because the virus persists in renal tissues, and while the infection is often dormant and benign, it can lead to BKVAN, which threatens graft survival. Several factors increase the risk of BKV, including human leukocyte antigen (HLA) mismatch, deceased donors, acute rejection, stent use, male recipients, older age, and the use of specific immunosuppressants such as anti-thymocyte globulin (ATG) induction combined with tacrolimus (TAC) or mycophenolate mofetil (MMF). The primary method for diagnosing BKVAN is renal biopsy, where viral cytopathic changes and Simian Virus 40 immunohistochemistry confirm the presence of the virus and assess chronic kidney damage.

The primary strategy for managing BKVAN is reducing immunosuppressive therapy, but this comes with the risk of acute rejection, which may jeopardize the survival of the transplanted kidney. Treatment for BKVAN include reducing doses or switching calcineurin inhibitors (CNI) such as TAC and cyclosporin (CSA), reducing MMF or azathioprine, switching to mammalian target of rapamycin (mTOR) inhibitors, or using antiviral agents like cidofovir, fluoroquinolones, and intravenous immunoglobulin (IV IgG) to clear or suppress the virus.

The eligibility criteria included patients who had primary or repeat kidney transplants from a deceased or living donor with documented BK viraemia, viruria, or biopsy-proven BKVAN. Patients were also included if they were receiving an intervention to reduce BK viraemia or prevents BKVAN, (included immunosuppression modification, antiviral therapies, antibiotics, mTOR inhibitors, and combination therapy). Only randomized controlled trials (RCTs) and quasi-RCTs were included in the review, and the primary outcomes assessed were the Standardized Outcomes in Nephrology including those related to graft survival, such as graft loss or rejection, and kidney function. Secondary outcome measured were the elimination of BK viruria or BK viraemia, BKVAN, infection (such as UTIs), cancer, cardiovascular disease, development of de novo DSA, death, and therapy-related adverse events.

For this review, a total of 12 RCTs with a combined 2,669 participants were analyzed. There was significant heterogeneity across studies including type of interventions, study durations (6 months to 5 years), and follow-up periods (8 months to 5 years), making it challenging to draw definitive conclusions. The risk of bias was often unclear, as many studies lacked sufficient information for accurate assessment. Only one of the 12 studies (Humar, 2013) adequately addressed all domains of risk of bias.

The results indicated that intensive screening was associated with reduced BKV persistence and improved graft survival compared to routine care. Fluoroquinolones appeared to reduce the risk of urinary tract infections (UTIs) and graft loss but had minimal impact on BK viraemia at one year and may increase the risk of tendonitis. The comparison between cyclosporin (CSA) and tacrolimus (TAC) showed that CSA may lower the risk of BK viraemia, but makes little or no difference to graft loss, BKVAN incidence, or malignancies. CSA was also associated with a reduced incidence of new-onset diabetes after transplantation (NODAT). Studies comparing MMF and azathioprine suggested that MMF had similar outcomes for graft survival and BK

viraemia but was associated with a lower risk of malignancy and death. The conversion of MMF or TAC to mTOR inhibitors showed uncertain benefits, with some evidence suggesting that mTOR inhibitors could increase mortality. In addition, the leflunomide derivative FK778 lowered BK viral load but worsened kidney function and increased the risk of hypertension.

The main takeaway from this systematic review is the importance of intensive screening protocols for early detection and prevention of BKVAN in the first two years post-kidney transplant. Comparisons between commonly used immunosuppressants showed no significant differences in BKVAN risk, and antiviral agents like fluoroquinolones or FK778 were shown to provide little benefit and potential adverse effects. The clinical implications are still somewhat uncertain as most of the evidence supporting these findings was of low to moderate certainty. This highlights the need for more high-quality RCTs on management of BK nephropathy in kidney transplantation to guide clinical practice.

Wajih Z, Karpe KM, Walters GD. Interventions for BK virus infection in kidney transplant recipients. Cochrane Database of Systematic Reviews 2024, Issue 10. Art. No.: CD013344. DOI: 10.1002/14651858.CD013344.pub2. Accessed 10 October 2024.