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Renal Dysfunction in a Cohort of Renal Transplant Recipients: Impact of BK Polyomavirus

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BACKGROUND

- BK Polyomavirus (BKPyV) may cause renal allograft dysfunction and premature graft loss.
- We investigated the relationship between BKPyV viraemia and renal dysfunction among renal transplant recipients enrolled in the The Management of Post-Transplant Infections in Collaborating Hospitals (MATCH) program, a large transplantation cohort from Rigshospitalet, Copenhagen.

OBJECTIVES

- To determine factors associated with BKPyV viraemia in a cohort of renal transplant recipients;
- To evaluate the association between detection of BKPyV viraemia and the risk of poor renal outcome.

METHODS

- The MATCH program was introduced at Rigshospitalet in Copenhagen, Denmark in 2011, with the aim to reduce the risk of severe viral diseases in transplant recipients. MATCH constitutes a platform for collaboration between the transplantation units and the Department of Infectious Diseases, and the associated database contains data on a large cohort of consecutive transplant recipients of both solid organ transplantation and haematopoietic stem cell transplantation.
- Renal transplant recipients enrolled in MATCH after Oct 1st2011 were included.
- Patients with primary graft non-function were excluded.
- BKPyV DNA was tested for screening in blood 60, 90, 179 and 270d post-transplant and on clinical suspicion.
- Survival analysis by means of Kaplan-Meier curves and Cox regression models was performed. Cox models with baseline covariates were used to identify factors independently associated with a composite endpoint of eGFR <40, confirmed 25% eGFR decrease, graft loss, or death. Time zero for this survival analysis was the time of first BKPyV test.

Box 1. Factors adjusted for in multivariable analyses

Recipient-related factors
- age at transplantation
- gender
- diabetes mellitus
- calendar year of transplantation
- renal replacement therapy modality prior to transplantation: peritoneal, hemodialysis, pre-emptive

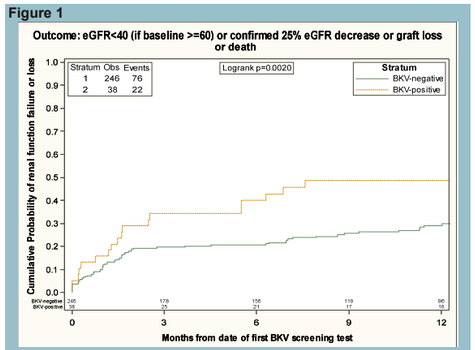
Donor/graft-related factors
- living versus dead donor
- donor age
- AB or DR mismatches
- ABO compatibility
- time of cold ischemia
- delay in graft function

Induction therapy
- basiliximab alone
- anti-thymocyte globulin
- combination of rituximab, basiliximab and intravenous immunoglobulin

Occurrence of rejection
- Yes or no
- If yes, antibody-mediated rejection vs not antibody-mediated
- Banff borderline, grade I or grade II)

Occurrence of rejection & chosen rejection therapy
- prednisolone-based therapy
- intravenous immunoglobulin-based therapy
- anti-thymocyte globulin

Figure 1



People with BKPyV viraemia had a greater risk of poor renal outcome (univariable Kaplan-Meier analysis).
Results were confirmed in a multivariable Cox regression model (adjusted Hazard Ratios, 95% CI: 1.99, 1.22-3.24, p=0.006, see **Table 1**)

METHODS (CONT.)

- Separate models assessed factors associated with BK viremia, investigating recipient- and donor-related factors, induction immunosuppressive therapy, and rejection as covariates (**Box 1**). Time zero was defined as 42d post transplantation to allow renal function stabilization.

RESULTS

- 322 patients were included. 87 had BKPyV viraemia . 98 developed the composite endpoint (1 developed eGFR <40, 95 a confirmed 25% eGFR decrease [6 of whom died and 2 lost the graft], and 2 died).
- Annual incidence of BKPyV viraemia viremia was stable over the study period ranging from 33.0 to 33.6 /100 PYFU (p= 0.98).
- Participants with BKPyV viraemia had a higher risk of developing the composite endpoint (2.06, 1.25-3.39, p=0.002)(**Figure 1**).
- Factors independently associated with detection of BKPyV viraemia were antibody-mediated rejection (adjusted hazards ratio [aHR], 95% CI: 2.68, 0.97-7.39, p=0.057) and immunoglobulin(IVIG)-based treatment for rejection (3.20, 0.99-10.42, p=0.053) (**Figure 2**).
- Other factors independently associated with the composite endpoint of poor renal function were use of Rituximab+IVIG+Basiliximab during induction (1.89, 1.12-3.18, p=0.02, vs. Basiliximab alone) and recipient's age (1.15, 0.98-1.34, p=0.09 , per 10y older) (**Table 1**).

CONCLUSIONS

- Approximately one third of those who underwent a kidney transplantation at Rigshospitalet had detectable BKPyV viraemia by 1 year of transplantation.
- Early detection of BKPyV viraemia was associated with a higher risk of renal dysfunction, graft loss and death in our cohort.
- Antibody-mediated rejection and immunoglobulin-based treatment for rejection appeared to increase the risk of BKPyV viraemia.

ACKNOWLEDGEMENTS
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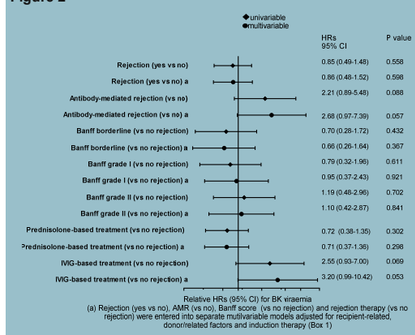
Figure 2



Association between rejection and risk of BKPyV viraemia from fitting a Cox regression model adjusted for factors listed in **Box 1**; MATCH cohort (n=322)

Table 1

	Unadjusted HR (95% CI)	p-value	Adjusted* HR (95% CI)	p-value
BKPyV viraemia				
Positive vs. Negative	2.08 (1.29, 3.34)	0.003	1.99 (1.22, 3.24)	0.006
Age of recipient at transplantation				
per 10 years older	1.23 (1.05, 1.43)	0.009	1.15 (0.98, 1.34)	0.093
Induction therapy				
Basiliximab	1.00		1.00	
Rituximab+IVIG+Basiliximab	1.95 (1.17, 3.25)	0.010	1.89 (1.12, 3.18)	0.017
Anti-thymocyte globulin	1.21 (0.49, 3.00)	0.677	0.94 (0.35, 2.48)	0.896
Rejection				
Yes vs. No	1.17 (0.71, 1.91)	0.535	1.01 (0.60, 1.69)	0.983
Age of donor				
per 10 years older	1.25 (1.07, 1.46)	0.004	1.14 (0.96, 1.36)	0.129
Delay in graft function				
1-7 days vs. no delay	1.36 (0.74, 2.51)	0.320	1.47 (0.79, 2.73)	0.226
8-42 days vs. no delay	1.41 (0.73, 2.73)	0.311	1.37 (0.65, 2.85)	0.407

Hazard ratios of poor renal outcome from fitting a Cox regression model adjusting for factors listed in **Box 1**

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