BK Virus Viremia and Nephropathy in Kidney Transplant Recipients: Assessment of Predictive Factors, Low Dose Tacrolimus Plus Everolimus Effects and Viral Load

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Abstract

Background

BK virus viremia or nephropathy is very important for graft survival and functions in renal transplant recipients. We aimed to determine the predictive factors of BK virus viremia or nephropathy, to discuss the effect of swiching to low dose tacrolimus plus everolimus and the viral load in kidney transplant patients.

Methods

3654 kidney transplant recipients were included in the study. Firstly, the patients were divided into two groups (Group 1: BKV (-) (n = 3525, 96.5%), Group 2: BKV viremia (+) (n = 129, viremia 3.5%, nephropathy 1%) were evaluated. Secondly, patients with BKV viremia / BKPyVAN were divided into two groups according to immunosuppressive changes (Group 2a: swiching to low dose tacrolimus plus everolimus (n = 54, 41.9%), Group 2b: swiching to other immunosuppressive protocols (n = 75, 58.1%) were evaluated. Thirdly, the cut-off value of the viral load amount ($\geq 10^4$ and $< 10^4$) was discussed.

Results

History of rejection, elderly recipient, cadaveric transplantation, use of anti-thymocyte globulin, tacrolimus and CMV viremia are predictive factors for BKV development. It was shown that the rate of viremia/nephropathy was highest in tacrolimus plus mycophenolic acid protocols, The use of low dose Tacrolimus plus Everolimus as an exchange protocol after BKV viremia or BKPyVAN had a positive effect on the outcomes, a viral load $\geq 10^4$ was shown to be a significant cut-off value in terms of nephropathy development and graft survival.

Conclusion

BK virus development in kidney transplant recipients is multifactorial and it was thought that preventive measures may be more important than treatment.

Background

BK virus (BKV) seems to be transmitted via respiratory and oral routes and causes latent infection by colonizing the urinary system. The seroprevalence is over 90% in the first decade of life[1, 2]. BK virus reactivation can occur in the setting of immunosuppression, and it manifests as viruria (viral load > 107 in 30–50% of patients), viremia (viral load ≥ 104 in 10–30%), and BK polyomavirus associated nephropathy (BKPyVAN in 1–10%). BKPyVAN leads to graft loss (10–90%) within approximately five years [3–5]. Since there is no effective antiviral treatment, early detection and early interventions are very important in

prognosis[6–8]. For this reason, BKV DNA tracking is performed with different center-based protocols in the post-transplant periods[6, 7, 9]. IS reduction continues to be the cornerstone of BKPyVAN treatment[7, 8, 10, 11].

Risk factors for BK reactivation include acute rejection (AR) episodes and their treatment number of mismatch, ureteric stents, use of high-dose IS, use of calcineurin inhibitors (CNI; especially tacrolimus-TAC) and mycophenolic acid (MPA), female donor, male recipient, cadaveric transplants, retransplants, ischemic or immunological damage to the graft, high BKV-specific antibody titers in the donor, low or absent BKV-specific antibody titers in the recipient, and elderly recipients. Cyclosporine (CSA) poses a very low risk in terms of BKV reactivation compared to TAC and it is even known to have an inhibitory effect on viral replication[12, 13]. Although the effect of mammalian target of rapamycin inhibitors (m-TORi) on BKV is not known exactly, it is known that the risk is lower than TAC and it is among the preferred protocols because it reduces CNI exposure. BKPyVAN is usually seen within one year after transplantation, and in the late period, it often develops due to high-dose IS use[14].

A viral load ≥ 4 log10/mL is considered a cut-off for nephropathy and it is recommended to reduce IS [15]. However, different studies suggest that this value underestimated the diagnosis of BKPyVAN. It has been reported that there are cases where nephropathy was diagnosed with BKV DNA < 10^4 [16, 17]. Therefore, the issue of significant viral load for nephropathy is still open to debate.

In our study, we aimed to investigate predictors of viremia and BKPyVAN, to discuss the effectiveness of swiching to low dose TAC plus everolimus (EVE) and the cut-off value of viral load (≥- <4 log10/mL).

Methods

The study was approved by the Akdeniz University Medical Faculty Clinical Research Ethics Committee (Date: 21.10.2020, the decision code: 2012-KAEK-20, the decision number: KAEK-831). Three thousand six hundred fifty-four kidney transplant patients were included in the study. Firstly, the patients were divided into two groups and analyzed. Group 1: BKV (-) (n=3525, 96.5%) and Group 2: BKV viremia (+) (n=129, viremia 3.5%, nephropathy 1%). The demographic data of the groups, donor types, chronic kidney disease (CKD) etiology, renal replacement therapy (RRT) modalities and panel reactive antibody (PRA) titers are given in Table 1. Logistic regression analysis was performed to determine predictive factors for BKV viremia/nephropathy development among the groups. BKPyVAN development rates were determined based on immunosuppressive protocols (ISP; induction, maintenance). Graft functions (serum creatinine-Cr and glomerular filtration rate-GFR at the last control), graft and patient survival rates, AR attacks and other clinical parameters were compared. Besides, patients were grouped according to AR attack presence only before ISP intervention and graft survival rates and functions were compared.

Secondly, the results of ISP modifications were evaluated. The patients were divided into two groups and analyzed. Group 2a: Swiching to low dose TAC plus EVE (n = 54, 41.9%), Group 2b: Swiching to other ISPs (n = 75, 58.1%). Demographic, immunological, AR rates, graft functions, graft and patient survival rates,

mean BKV DNA levels and other clinical results were compared. Graft functions were evaluated by serum Cr level and GFR measurement. These parameters were recorded when the ISP was changed due to BKV (1st measurement), the viral load fell below this value in those with $\geq 10^4$, the BKV titer became negative or decreased 50% compared to the initial value in those with $<10^4$ (2nd measurement) (Group A / B, respectively: 49 (90.7%) / 27 (36%) - $<10^4$ respectively: 5 (9.3%) / 48 (64%), p: <0.001) and all the patients had the last control (3rd measurement).

Thirdly, all patients were grouped according to viral load amounts ($<10^4$- $\geq 10^4$) and compared in terms of all clinical outcomes. Groups 2a and 2b were also compared in terms of viral load amount and pathological findings. Patients with viral load $\geq 10^4$ (n = 76, Group 2a/ 2b: 49/27) were also evaluated. Those with viral load $<10^4$ were grouped as those with and without ISP change, and the results were compared.

BKV viremia follow-up is performed every month for the first six months after transplantation, every three months in months 6-12, every six months in years 1-2 and once a year after that. The test is repeated in patients with viremia until resolution or last follow-up. Dose reduction-interruption in MPA derivatives, reduction of CNI dose with MPA, changing TAC to CSA ± MPA dose reduction/interruption, switch to low-dose TAC plus EVE combination (TAC: 2-4 ng / mL, EVE: 4-7 ng / mL) and only EVE plus prednisolone modifications are made. These modifications can be made as multiple changes according to BKV follow-up. Cidofovir in resistant cases, IV immunoglobulin, especially in patients accompanied by rejection and leflunomide in a resistant case (only one patient), were added to the treatment. During the BKV follow-up, patients who developed AR were given rejection therapy, and they were followed up by returning to the BKV strategy. The diagnosis was confirmed with a kidney biopsy in patients who did not respond to ISP changes, had very high BKV titer and developed graft dysfunction.

Low-dose CNI + mTORi protocols are frequently used in our clinic. The target CNI level is reduced by 20-40% in these patients compared to classical CNI + MPA protocols. In maintenance, it is modified based on the GFR and immunological risk group of the patient.

Statistical analyses:

Study data were analyzed with SPSS version 23.0. Normality analysis was evaluated using the Shapiro Wilk test. A comparison of the mean of the data (mean ± SD) with normal distribution was made by Student-t-test (parametric test), and those that did not have a normal distribution (median (minimum-maximum)) were made with the Mann-Whitney U test (non-parametric test). Continuous variables were given as mean ± SD and categorical variables as percentages. A relationship between categorical variables was evaluated with the Chi-Square test (Fisher's Exact test with minimum expected count <5, Continuity Correction for 5≤- <25, Pearson Chi-Square value for ≥25). Logistic regression analysis was performed to determine the predictive factors in BKV development. Survival analyzes were evaluated by Kaplan-Meier survival curves and compared using the log-rang test. All hypotheses were formed as two-tailed and an alpha critical value of 0.05 was considered significant.

Results

Comparison of group 1 and 2:

BKV viremia rate was found to be 3.5% (nephropathy rate 1%). There was no difference between the groups in terms of gender, CKD etiology, donor age, viral hepatitis, mismatch numbers (p: 0.980), rate of MPA and EVE use (Table 1). Among the clinical outcomes, the need for postoperative hemodialysis (HD), chronic allograft dysfunction (CAD), development of new-onset diabetes mellitus after transplantation, malignancy development rates, patient and graft loss rates, patient survival rates and serum Cr and GFR mean value at the last control were found to be similar (Table 2). In the 2nd group, it was determined that 34 (26.4%) of 129 patients developed BKPyVAN, 19 (14.7%) had graft loss and 7 (5.5%) of them were due to BKPyVAN.

Recipient age, body mass index, cadaveric transplant rate, anti-thymocyte globulin (ATG) use rate in induction therapy, TAC / MPA / prednisolone use rate (n = 120, 93%), the rates of AR (humoral/cellular), delayed graft function (DGF), cytomegalovirus (CMV) viremia and vesicoureteral reflux rates to transplant kidney were higher in group 2. Graft survival rates were shown to be lower in the BKV group (group 1 and 2, respectively, 1st-3rd-5th-10th year; 95.4% / 96.9- 92.8 / 89.8- 90.4 / 78.7- 85.7 / 65, p: 0.01). While TAC was used more, CSA and sirolimus (SRL) less in the second group, MPA and EVE were used with similar rates. It was shown that in all patients who used low-dose CNI + m-TORi (n=8, 6,2%), the viremia / BKPyVAN ratio was lower and the ratio was significantly higher in the TAC + MPA protocol (Table 1).

In logistic regression analysis, the presence of AR, elderly recipient, cadaveric transplantation, ATG and TAC use and, CMV viremia were shown to be predictive factors for BKV development (Table 3).

Patients who had AR before ISP change (AR +/-, n = 33/96, respectively) had lower graft survival rates (1st-3rd-5th-10th year, respectively, AR (+): %93/84/72/43, AR (-): 97/93/84/77, p: 0.045), and graft functions (Cr values higher in all three measurements, lower GFR levels, p: <0.001) were shown to be worse.

Group 2a (swiching to low dose TAC plus EVE, n=54) / Group 2b (swiching to others ISP, n=75) comparisons;

It was found that there was no difference between the groups in terms of demographic and immunological parameters. However, CKD etiologies, cadaveric transplant rates, mismatch numbers, RRT modalities, induction therapies, TAC and ATG usage rates, CAD, DGF, CMV rates, graft / patient survival rates were similar for the two groups. BKPyVAN ratio was higher in group 2a (Group 2a/ 2b, respectively 23 (42.6%)/ 11 (14.7%), p: <0.001). Graft losses were found in 9 patients in group 2a (in 5 (55.5%) patients were due to BKPyVAN) and 10 patients in group 2b (in 2 patients (20%) were due to BKPyVAN) (p: 0.507). It was observed that BKV DNA levels showed a fluctuating course: higher in group 2b at the first measurements, similar between the groups in the following measurements, and higher in group 2a at the last measurement (Figure 1).

In terms of graft functions, the 1st and 3rd measurements were similar, while the second measurements showed worse graft functions in the group 2a. In summary, it was found that graft functions were impaired after changing the protocol in group 2a, but there was no difference between the last controls (long term).

The graft loss rates (Group 2a-2b, respectively, 9 (16.7%) - 10 (13.3%), p: 0.598) and biopsy findings (glomerulitis, interstitial inflammation, tubulitis, chronic glomerulopathy, interstitial fibrosis, tubular atrophy, SV40 (+), C4d (+), transplant glomerulopathy) were found to be similar between the groups. The rate of using cidofovir was higher in group 2a (Group 2a/ 2b, respectively 18.5%/ 5.3%, p: 0.018). Before the ISP change, the AR rates were found to be high in the EVE arm for both 129 patients (Group 2a/2b; 38.9%/ 16%, p: 0.003) and the patients with PCR $\geq 10^4$ (Group 2a/2b; 36.7%/ 7.4%, p: 0.005, respectively). After the ISP change, the AR rates were similar (Group A-B 13% / 5.3%, p: 0.2, respectively).

Comparisons of those with viral load $\geq 10^4$- $<10^4$:

In the analyzes carried out independently from the ISP, while the graft survival rates were lower in those with $\geq 10^4$ than those with $<10^4$ (respectively 1st-3rd-5th-10th year $\geq 10^4$/ $<10^4$; 94/ 98- 88/ 96- 73/ 91- 41/ 85, p: 0.017), the graft functions were shown to be similar between the groups in all three measurements. It was found that BKPyVAN did not develop in patients with BKV DNA $<10^4$, whereas it developed in 34 (44.7%) patients (p: <0.001) in those with $\geq 10^4$. It was determined that 15 of the graft losses were developed in patients with viral load $\geq 10^4$; 4 were the patients with viral load $<10^4$ (rejection in 2 patients, CAD in 1 patient, patient loss in 1 patient). There was no significant difference between rates of graft loss due to BKPyVAN ($\geq 10^4$/ $<10^4$; 7 (46.7%) / 0, p: 0.245, respectively).

In the subgroup analyses of 76 patients with only BKV PCR $\geq 10^4$ (Group 2a/ 2b: 49/27); demographic data, graft / patient survival rates, graft function, and other clinical outcomes were similar between the groups. The negative, decreased to $<10^4$ and remained $\geq 10^4$ rates of BKV DNA levels after ISP change were similar in group 2a/2b (group 2a (36.7- 30.6-32.7%, respectively) / 2b (40.7- 29)). , 6- 29.6%), p: 0.937). Acute rejection rates were higher in Group 2a before the ISP change (Group 2a/ 2b 36.7% / 7.4%, p: 0.005), and (Group 2a/ 2b, respectively 12.2% / 3.7%). p: 0.410) were found to be similar after ISP change.

Fifty-three patients with BKV PCR $<10^4$ only (Group 2a/ 2b: 5/48); were divided into subgroups as the patients without ISP change (n = 21) and those with all ISP change (n = 32). Demographic data, mean PCR levels, graft survival rates, graft functions, rejection rates and all other clinical outcome rates were shown to be similar between the groups.

Discussion

In our study, AR attack, elderly recipient, cadaveric transplant, ATG, TAC use and CMV viremia were shown to be predictive in the development of BKV viremia / BKPyVAN. It was found that the risk was the highest

in the classical TAC + MPA protocol and the rate was lower in those using low dose CNI + mTORi. The use of low dose Tacrolimus plus Everolimus as an exchange protocol after BKV viremia or BKPyVAN had a positive effect on the outcomes. Graft survival rates were lower and the graft functions were similar in those with viral load $\geq 10^4$. There was no graft loss due to BKPyVAN and ISP modifications did not change the result in those with viral load $< 10^4$. Graft survival rates and graft functions were worse in those who had a rejection attack before the IS protocol change.

It is known that the main factor in BKV viremia/ BKPyVAN is intensive IS use, especially TAC is associated with increased risk, but it develops with different rates in almost all IS protocols, and the rate is lower in patients using m-TORi [8, 13, 18–22]. Also, older recipient age, male gender, the high number of mismatch, AR, ureteral stents, ischemia, DGF and transplantation from seropositive donors to the negative recipient are considered as other risk factors [23–26].

In our study, BKV viremia/ BKPyVAN was developed more in cadaveric transplants, elderly recipients, DGF and vesicoureteral reflux to the transplanted kidney, and patients with a high AR rate, and the graft survival rate were lower in this group. BKV viremia/ BKPyVAN ratio was very high in patients using TAC-based IS and lower in patients using CSA or m-TORi. It was also found that the rate was very low in all low-dose CNI + m-TORi protocols. Our study supported the literature with these results and especially contributed to the results of low-dose CNI + m-TORi protocols.

In the study of Brennan et al., it has been shown that BKV viremia rate is higher in TAC users compared to CSA, preemptive reduction of IS provides viremia clearance and prevents the development of nephropathy[13]. In the study of Bischof et al., it has been shown that decreasing the TAC dose increases BKV clearance, and this result is more significant with the reduction of the MPA dose and high viral load is a poor prognostic factor [3]. Other studies have shown that the frequency of humoral rejection increases due to MPA dose reduction alone [3, 27, 28]. In the DIRECT study, it was shown that the frequency of BKV viruria, viremia and nephropathy was lower in the CSA arm than TAC. [18, 29]. Many studies show that BKV risk is higher in TAC + MPA protocols than other regimens [8, 13, 30]. In our study, it was shown that BKV viremia/nephropathy was developed due to tacrolimus-based and CSA-based ISPs in 96.9% and only 3.1% of the patients, respectively. However, it has also been shown that IS modification in BKV DNA $< 10^4$ does not affect the result. Studies with more patients should investigate this result.

Switching from classical CNI + MPA protocols to mTORi combinations is an important treatment alternative in patients with BKV viremia/nephropathy. In this way, although CNI/ MPA doses have been reduced, there is no generally accepted effective protocol in this regard [31–34]. In the study of Mühlbacher et al., IS treatments of patients who developed BKV nephropathy were changed to m-TORi-based regimens and low-dose cidofovir was added. As a result, it has been shown that viral clearance was achieved significantly, had a positive contribution to graft survival and functions, and three of the nine graft losses were due to BKPyVAN. [35]. In the study of Moscarelli et al., low-dose cyclosporine plus everolimus was compared with standard-dose cyclosporine + mycophenolic acid in terms of BKV viremia, and it was shown that viremia, nephropathy and graft loss rates were lower in the everolimus arm [19]. In

our study, none of the 141 patients who were low-dose cyclosporine plus everolimus developed BKV viremia or BKPyVAN. İt was also shown that BKV viremia/ BKPyVAN development rates were significantly lower in all patients using low dose CNI (Tac/ CSA) + mTORi than standard-dose TAC + MPA (in postoperative initial ISP).

In the study, in group 2a (switching to low dose Tac plus Eve group after BKV viremia or BKPyVAN) the rates of BKPyVAN, rejection before ISP change, use of cidofovir and viral load were higher than other ISP change groups (Group 2b). Despite these poor prognostic factors, graft functions at the last follow-up, graft survival rates, and post-exchange rejection rates were found to be similar between groups. These results indirectly showed that the use of low dose Tacrolimus plus Everolimus in patients with BKV viremia or BKPyVAN had a positive effect on the outcomes. Increasing rejection and graft dysfunction rates after switching to less effective ISPs in patients with BKV are the most important problems. Although it was mostly used in patients with poor prognosis in our study, rejection rates did not increase and graft functions were preserved after switching to low dose Tac plus Eve. Our study is very important in this respect and contributed to the literature.

In the study of Bayraktar et al., it was shown that there is no relationship between ATG use and BKV nephropathy [36]. This result was thought to be related to the patients included in the study. In our study, it has been shown that the use of ATG is one of the most important risk factors for BKV, as in many other studies.

In the study of Vu et al., intravenous immunoglobulin (IVIG) was given to 30 patients with BKV viremia/ BKPyVAN resistant to IS reduction and leflunomide treatment, and viral clearance was achieved in 27 patients, and this result showed that IVIG use was effective in resistant cases [37]. In our study, IVIG and leflunomide were given to a patient resistant to all ISP changes, but the result was not obtained and graft loss occurred.

It is generally accepted that a viral load of $\geq 10^4$ copies/ mL predicts nephropathy [8, 10]. However, studies show that nephropathy develops in amounts below this value and emphasizes that this value underestimates BKPyVAN [16, 38]. Our study showed that graft survival rates were lower in those with BKV DNA $\geq 10^4$ than those with $< 10^4$, and the graft functions and all other clinical outcomes were similar. It has also been shown that the BKPyVAN ratio is significantly higher in those with BKV DNA $\geq 10^4$, but the graft loss rates due to nephropathy were similar. Although this result showed that nephropathy frequency would increase with increasing viral load, it pointed out that it could be prevented from causing graft loss with appropriate IS modification.

In conclusion, in the development of BKV viremia/BKPyVAN, AR attack, elderly recipient, cadaveric transplant, ATG and TAC use, and CMV viremia are predictive. While the risk is the highest in the classical TAC + MPA protocol, the rate is lower in those using low dose CNI + mTORi. The use of low dose Tacrolimus plus Everolimus as an exchange protocol after BKV viremia or BKPyVAN had a positive effect

on the outcomes. It has been shown that BKV DNA ≥ 10^4 is predictive in terms of graft survival and BKPyVAN development.

Declarations

It is a retrospective study and data usage permission was obtained (before ethics committee approval).

The authors are declare no conflict of interest.

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Authorship:

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Tables

Table 1. Comparison of demographic and other features in the groups

Parameter	BKV(-)	BK viremia/BKPyVAN	P Value
Number	3525(96,5%)	129(3,5%/1%)	
Age_R	36,9±12,8	41,2±13,2	<0,001
Age_D	43,2±13,3	42,1±13,7	0,598
$Gender_R$(M/F)	2358/1167	91/38	0,387
$Gender_D$(M/F)	1721/1802	53/76	0,083
BMI_R	25,4±3,3	26,5±3,4	0,009
BMI_D	26,7±9,2	26±4,5	0,059
Donor type(C/L)	546(15,5%)/2979(84,5%)	31(24%)/98(76%)	0,009
CKD Etiology			0,104
DM	262(8%)	19(14,7%)	
HT	552(16,9%)	17(13,2%)	
GN	442(13,5%)	16(12,4%)	
Cystic RD	158(4,8%)	5(3,9%)	
Urologic	438(13,4%)	21(16,3%)	
Unknown	948(29%)	36(27,9%)	
Other	725(14,4%)	15(11,6%)	
RRT Type			<0,001
Pre-emptive	728(20,7%)	45(34,9%)	
HD	2244(63,7%)	64(49,6%)	
PD	412(11,7%)	10(7,8%)	
HD+PD	141(4%)	10(7,8%)	
PRA titers	Median(min-max)-Mean	Median(min-max)-Mean	
PRA Class I (preop.)	0(0-100)-11,6	0(0-100)-5,3	0,016
PRA Class I (last)	0(0-100)-15,8	0(0-98)-2,9	<0,001
PRA Class II (preop.)	0(0-100)-20,8	0(0-100)-8,2	<0,001
PRA Class II (last)	0(0-100)-28,3	0(0-96)-6,1	<0,001
ISP			<0,001

TAC+MPA	2542 (72,1%)	120(93%)	
CSA+MPA	494(14%)	1(0,8%)	
TAC+SRL	102(2,9%)	0(0%)	
TAC+EVE	69(2%)	5(3,9%)	
CSA+EVE	141(4%)	0(0%)	
CSA+SRL	177(5%)	3(2,3%)	
Induction therapy			<0,001
No	812(23%)	16(12,4%)	
Daclizumab	162(4,6%)	0(0%)	
Basiliximab	1650(46,8%)	44(34,1%)	
ATG	871(24,7%)	66(51,2%)	
Basiliximab+ATG	30(0,9%)	3(2,3%)	
ATG(+)	901(25,6%)	69(53,5%)	<0,001
TAC(+)	2717(77,1%)	125(96,9%)	<0,001
CSA(+)	808(22,9%)	4(3,1%)	<0,001
MPA(+)	3501(99,3%)	129(100%)	1
EVE(+)	222(6,3%)	5(3,9%)	0,263
SRL(+)	274(7,8%)	3(2,3%)	0,022

R:Recipient; D:Donor; C: Cadaveric; M: Male; F: Female; CKD: Chronic Kidney Disease; DM: Diabetes Mellitus; HT: Hypertension; GN: Glomerulonephritis; RD: Renal Disease; HD: Hemodialysis; PD: Peritoneal Dialysis; PRA: Panel Reactive Antibody; ISP: Immunosupressive Protocol; TAC: Tacrolimus; MPA: Mycophenolic Acid; CSA: Cyclosporine; EVE: Everolimus; SRL: Sirolimus; ATG: Anti-Timocyte Globuline

Table 2. Comparison of clinical outcomes and graft functions in the groups

Parameter	BKV(-)	BK viremia/BKPyVAN	P Value
AR	15,3%	31%	<0,001
None	2986(84,7%)	89(69%)	
Early ABMR	31(0,9%)	6(4,7%)	
Late ABMR	12(0,3%)	3(2,3%)	
c-aABMR	73(2,1%)	5(3,9%)	
TCMR	423(12%)	26(20,2%)	
PP (postop.)	215(6,1%)	18(14%)	<0,001
HD (postop.)	206(6,3%)	10(7,8%)	0,519
CAD	206(5,8%)	4(3,1%)	0,194
DGF	245(7%)	14(10,9%)	0,018
PTDM	358(10,2%)	16(12,4%)	0,408
PTTm	55(1,6%)	5(3,9%)	0,057
CMV	72(2%)	8(6,2%)	0,007
VUR (Trans.Kid.)	12(0,3%)	3(2,3%)	0,001
P. Loss	106(3%)	3(2,3%)	1
G.Loss	492(14%)	19(14,7%)	0,804
Cr (last control)	1,9±1,7	1,89±1,53	0,375
GFR (last control)	62,4±30,8	60,1±31	0,478
Graft survival			0,01
1.year	95,4%	96,9%	
3.year	92,8%	89,8%	
5.year	90,4%	78,7%	
10.year	85,7%	65%	

AR: Acute Rejection; ABMR: Antibody Mediated Rejection; c-aABMR: Chronic-active ABMR; TCMR: T-Cell Mediated Rejection; PP: Plasmapheresis; HD: Hemodialysis; CAD: Chronic Allograft Dysfunction; DGF: Delayed Graft Function; PTDM: Post-Transplant Diabetes Mellitus; PTTm: Post-Transplant Tumor; CMV: Cytomegalovirus; VUR: Vesicoureteral Reflux; P: Patient; G: Graft; Cr: Creatinine; GFR: Glomerular Filtration Rate

Table 3. The outcomes of logistic regression analysis for predictor factors of BK viremia and BKPyVAN

Parameters	B	SE	Odds ratio	Con.Interval	P value
Age_R	0,026	0,007	1,026	1,011-1,041	0,001
AR	-0,914	0,196	0,401	0,273-0,589	<0,001
Donor type (C/L)	0,718	0,227	2,050	1,315-3,197	0,002
ATG(+)	-1,009	0,185	0,365	0,254-0,524	<0,001
TAC(+)	-1,998	0,529	0,136	0,048-0,383	<0,001
CMV(+)	-1,134	0,407	0,322	0,145-0,714	0,005

R: Recipient; AR: Acute Rejection; C: Cadaveric; L: Living; ATG: Anti-Timocyte Globuline; TAC: Tacrolimus; AMV: Cytomegalovirus

Figures

Figure 1. The comparison of the levels of serum mean BKV DNA in the groups

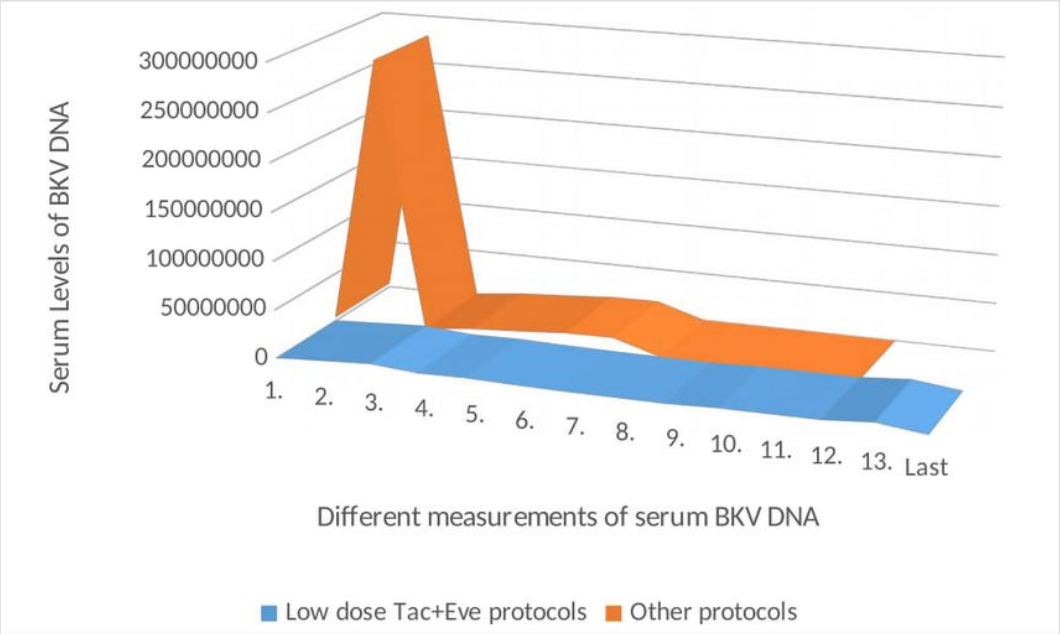

Figure 1

See image above for figure legend