Nephrol Dial Transplant (2017) 32: 1244–1250
doi: 10.1093/ndt/gfv375
Advance Access publication 6 November 2015

ndt
Nephrology Dialysis Transplantation

Original Articles

The clinicopathological relevance of pretransplant anti-angiotensin II type 1 receptor antibodies in renal transplantation

Juhan Lee[1], Kyu Ha Huh[1], Yongjung Park[2,3], Borae G. Park[2], Jaeseok Yang[4], Jong Cheol Jeong[4], Joongyup Lee[5], Jae Berm Park[6], Jang-Hee Cho[7], Sik Lee[8], Han Ro[9], Seung-Yeup Han[10], Myoung Soo Kim[1], Yu Seun Kim[1], Sung Joo Kim[6], Chan-Duck Kim[7], Wookyung Chung[9], Sung-Bae Park[10] and Curie Ahn[4,11], KNOW-KT on behalf of the Study Group

[1]Department of Surgery, Yonsei University College of Medicine, Seoul, Republic of Korea, [2]Department of Laboratory Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea, [3]Department of Laboratory Medicine, NHIC Medical Center, Ilsan Hospital, Goyang, Republic of Korea, [4]Transplantation Center, Seoul National University Hospital, Seoul, Republic of Korea, [5]Medical Research Collaborating Center, Seoul National University Hospital, Seoul, Republic of Korea, [6]Department of Surgery, Sungkyunkwan University, Seoul Samsung Medical Center, Seoul, Republic of Korea, [7]Department of Internal Medicine, Kyungpook National University Hospital, Daegu, Republic of Korea, [8]Department of Internal Medicine, Chonbuk National University Hospital, Jeonju, Republic of Korea, [9]Department of Internal Medicine, Gachon University, Gil Hospital, Incheon, Republic of Korea, [10]Department of Internal Medicine, Keimyung University, Dongsan Medical Center, Daegu, Republic of Korea and [11]Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Republic of Korea

Correspondence and offprint requests to: Kyu Ha Huh; E-mail: khhuh@yuhs.ac

ABSTRACT

Background: Anti-angiotensin II type 1 receptor antibodies (AT1R-Abs) have been suggested as a risk factor for graft failure and acute rejection (AR). However, the prevalence and clinical significance of pretransplant AT1R-Abs have seldom been evaluated in Asia.

Methods: In this multicenter, observational cohort study, we tested the AT1R-Abs in pretransplant serum samples obtained from 166 kidney transplant recipients. Statistical analysis was used to set a threshold AT1R-Abs level at 9.05 U/mL.

Results: Pretransplant AT1R-Abs were detected in 98/166 (59.0%) of the analyzed recipients. No graft loss or patient death was reported during the study period. AT1R-Abs (+) patients had a significantly higher incidence of biopsy-proven AR than AT1R-Abs (−) patients (27.6 versus 10.3%, P = 0.007). Recipients with pretransplant AT1R-Abs had a 3.2-fold higher risk of AR within a year of transplantation (P = 0.006). Five study subjects developed microcirculation inflammation (score ≥2). Four of them were presensitized to AT1R-Abs. In particular, three patients had a high titer of anti-AT1R-Abs (>22.7 U/mL).

Conclusions: Pretransplant AT1R-Abs is an independent risk factor for AR, especially acute cellular rejection, and is possibly associated with the risk of antibody-mediated injury. Pretransplant assessment of AT1R-Abs may be useful for stratifying immunologic risks.

Keywords: acute rejection, angiotensin II type 1 receptor antibody, antibody-mediated injury, pretransplant, renal transplantation

INTRODUCTION

Despite substantial improvements in immunosuppressive drugs, immune response remains a major challenge in kidney transplantation. In fact, both cellular and antibody-mediated rejections continue to adversely affect allograft survival [1, 2]. Human leukocyte antigen (HLA) is a critical target of the

recipient immune system, and the presence of antibodies against HLA is one of the most well-established risk factors of acute rejection (AR) and graft failure after organ transplantation. Recently devised solid-phase assays allow the accurate detection and quantification of donor-specific anti-HLA antibodies (DSA) [3]. However, not all DSA are associated with adverse clinical outcomes [4]. Furthermore, isolated cases have been described with the histologic features of antibody-mediated injury in the absence of DSA [5, 6]. Accordingly, the predicting of clinical outcome based on presensitization to HLA alone is unsound.

Anti-angiotensin II type 1 receptor antibodies (AT1R-Abs) have been proposed to constitute an alternative mechanism of graft injury and rejection beyond anti-HLA antibodies [5]. Furthermore, recent studies have reported associations between AT1R-Abs and clinical outcomes after kidney transplantation [7–9]. However, studies differed with respect to the prevalence of AT1R-Abs and its cut-off level. In addition, prior studies were performed in patients with limited ethnic composition. In fact, very few studies have evaluated the impact of AT1R-Abs on ARs in Asia [10, 11].

The aim of this study was to determine the prevalence of pretransplant AT1R-Abs and the impact of AT1R-Abs on clinicopathological outcomes after kidney transplantation.

MATERIALS AND METHODS

Patients

A subgroup of kidney transplant recipients enrolled in the KNOW-KT study were the subjects of this study. The KNOW-KT study is an ongoing multicenter, observational Korean cohort study designed to determine outcomes after kidney transplantation. Between June 2012 and February 2013, 250 patients were enrolled into the KNOW-KT study; the inclusion criteria used have been described previously [12]. A total of 166 recipients were included in the present study; 86 patients were excluded (47 administrative problems leading to insufficient data entries; 27 withdrawal of informed consent; 12 lost to follow-up). The analysis was conducted data extracted from the KNOW-KT database. Codes were used to ensure donor and recipient anonymity and AT1R-Abs analysis was performed in a blind manner.

Immunosuppression

Patients received induction therapy with either humanized anti-IL2R monoclonal antibody or rabbit anti-thymocyte globulin (ATG). Maintenance immunosuppression consisted of a calcineurin inhibitor (tacrolimus or cyclosporine A) with mycophenolate mofetil or mTOR inhibitor. Patients received a corticosteroid tapering from the day of surgery.

Measurement of pretransplant AT1R-Abs

AT1R-Abs levels (U/mL) in all available pretransplant serum samples from the KNOW-KT study bio-bank were measured retrospectively using AT1R assay kits (One Lambda, CA, USA) at the Department of Laboratory Medicine of Yonsei University Health System. All testing was conducted without knowledge of clinical data.

The detection range of the test was >2.5 U/mL with positive value set at >9.05 U/mL and negative at ≤9.05 U/mL. The optimal cut-off value of AT1R-Abs was determined by statistical analysis. Based on this cut-off value patients were assigned to AT1R-Abs (+) and AT1R-Abs (−) groups.

Crossmatch

Lymphocyte crossmatch was performed by both complement-dependent cytotoxicity (CDC)- and flow cytometry (FCM)-based methods. T- and B-cells were separated and the CDC crossmatch for detecting antibodies against donor T-cells was carried out based on the National Institutes of Health and anti-human globulin (AHG)-enhanced methods. The B-cell CDC crossmatch was done in warm phases. In order to exclude possible cases with donor-specific HLA antibodies (HLA DSA), only cases negative for both CDC crossmatch with donor T- and B-cells and FCM crossmatch with donor T-cells were included in this study.

Pretransplant anti-HLA antibody screening and DSA

Anti-HLA antibody screening was performed using Luminex panel reactive antibodies (PRA) assay kit (LIFECODES LifeScreen Deluxe and Class I and Class II ID, Immucor Transplant Diagnostics, Stamford, CT, USA) and was presented as %PRA. When the PRA test was positive, we checked the presence of the DSA by using Luminex single-antigen assay kits (LIFECODES LSA Class I and Class II). Luminex PRA assay was performed according to the manufacturer's instruction at the time of transplantation. The presence and antigen specificities of antibodies to HLA-A, -B, -DR and -DQ were determined. Only a limited number of single PRA results were included in this study.

Histological diagnosis for indication or protocol biopsies

All AR episodes were biopsy proven and were taken into account in the statistical analyses. ARs were classified as acute cellular rejection (ACR) or antibody-mediated rejection (AMR). We included both indication and protocol biopsies. Indication biopsies were defined as biopsies performed in a non-predetermined manner due to acute allograft dysfunction (creatinine increase or proteinuria), whereas protocol biopsies were defined as those performed at predetermined times, irrespective of graft function. Protocol biopsies were performed in accord with the policies of participating transplant centers. Allograft biopsies were read by a local pathologist and classified according to the revised Banff grading system. AR treatment was provided using local protocols.

AT1R-Abs in kidney transplantation was first described in association with AMR [5], and thus, antibody-mediated injury was evaluated using microcirculation inflammation (MI) scores, which were calculated by summing of glomerulitis and peritubular capillaritis scores.

Renal function

Serum creatinine was measured by an isotope-dilution mass spectrometry traceable method. Glomerular filtration rates

(GFR) were estimated by the four-variable Modification of Diet in Renal Disease (MDRD) formula. Routine laboratory assessments were performed at the local laboratory.

Statistical analysis

The optimal threshold AT1R-Abs level was statistically determined by maximizing the distance between corresponding ARs using Youden's index. The optimal cut-off level for AT1R-Abs was found to be 9.05 U/mL. MedCalc (version 12.7.0; MedCalc Software, Ostend, Belgium) was used for statistical analysis.

The Student's *t*-test was used to determine the significances of differences between the means of numerical variables between the AT1R-Abs (+) and AT1R-Abs (−) groups. The chi-square test with Fisher's exact test was used to compare nominal variables. Univariate and multivariate logistic regression analyses were performed to evaluate association with AR risk factors. Cox model analysis was adjusted for risk factors. The cumulative probabilities of AR were analyzed using a Kaplan–Meier graph and statistically compared using a log-rank test. The analysis was performed using SPSS software (version 20.0; SPSS Inc., Chicago, IL, USA), and P-values <0.05 were considered significant.

Table 1. Patient demographics in the two groups

	AT1R-Abs ≤9.05 U/mL 68 (41.0%)	AT1R-Abs >9.05 U/mL 98 (59.0%)	P-value
Recipient age, years	47.5 ± 12.5	44.5 ± 11.4	0.101
Male patients	50 (73.5%)	61 (62.2%)	0.129
Donor age, years	45.5 ± 11.4	46.2 ± 11.3	0.683
Male donor	43 (63.2%)	66 (67.3%)	0.583
Deceased donor	20 (29.4%)	34 (34.7%)	0.475
Original disease			
Diabetes	14 (20.6%)	11 (11.2%)	0.243
Hypertension	9 (13.2%)	13 (13.3%)	
Glomerulonephritis	19 (27.9%)	33 (33.7%)	
Polycystic kidney disease	5 (7.4%)	1 (1.0%)	
Others	21 (30.9%)	40 (40.8%)	
HLA-A mismatch	0.9 ± 0.7	0.9 ± 0.7	0.597
HLA-B mismatch	1.4 ± 0.7	1.3 ± 0.8	0.527
HLA-DR mismatch	1.1 ± 0.6	1.0 ± 0.8	0.303
Panel-reactive antibodies			
0–20%	49 (89.1%)	76 (90.5%)	0.749
20–80%	5 (9.1%)	7 (8.3%)	
80–100%	1 (1.8%)	1 (1.2%)	
Anti-donor HLA antibodies	5 (7.4%)	8 (8.2%)	0.453
ABO incompatible KT	5 (7.4%)	17 (17.3%)	0.062
Re-transplantation	3 (4.4%)	5 (5.1%)	>0.99
Induction therapy			
Anti-IL2R antibody	64 (94.1%)	96 (98.0%)	0.228
ATG	4 (5.9%)	2 (2.0%)	
Maintenance therapy			
TAC + MMF ± steroid	54 (79.4%)	73 (74.5%)	0.761
CsA + MMF ± steroid	8 (11.8%)	14 (14.3%)	
Others	6 (8.8%)	11 (11.2%)	

Results are expressed as mean ± standard deviation for continuous variables and as number (proportion) for categorical variables.
AT1R-Abs, angiotensin II type 1 receptor antibodies; ATG, anti-thymocyte globulin; HLA, human leukocyte antigen; KT, kidney transplantation; TAC, tacrolimus; MMF, mycophenolate mofetil; CsA, cyclosporine A.

Ethical consideration

The study was conducted according to the tenets of the Declaration of Helsinki. The KNOW-KT study was approved by the institutional review board of each participating center, and all participants in the study provided written informed consent. In addition, the KNOW-KT study was registered in an international clinical trial registry (NCT02042963 at http://www.clinicaltrials.gov) on 20 January 2014 [12].

RESULTS

Patient characteristics

Patient characteristics are summarized in Table 1. Patients were divided into two groups according to the level of AT1R-Abs: >9.05 U/mL, AT1R-Abs (+) and ≤9.05 U/mL, AT1R-Abs (−). Among the 166 kidney recipients, 98 patients (59%) were allocated to the AT1R-Abs (+) group. No statistical differences were observed between AT1R-Abs (+) and AT1R-Abs (−) groups in terms of recipient, donor and immunologic factors.

Immunosuppression consisted of anti-IL2R antibody or ATG, tacrolimus or cyclosporine A, steroid, mycophenolate mofetil and occasionally mTOR inhibitor. Immunosuppressive regimens were similar in the two groups.

Mean AT1R-Abs levels in pretransplant sera of AT1R (+) and (−) groups was 13.8 U/mL (±6.1) and 7.0 U/mL (±1.7), respectively. The distribution of AT1R-Abs levels is presented in Figure 1. Eight patients (5%) had an AT1R-Abs titer of >22.7 U/mL.

Pretransplant AT1R-Abs >9.05 U/mL is an independent risk factor for AR

The threshold value of AT1R-Abs estimated by maximizing the differences in AR was determined at 9.05 U/mL. Biopsy-proven acute rejection (BPAR) occurred in 27/98 (27.6%) patients in the AT1R (+) group and in 7/68 (10.3%) patients in the AT1R (−) group (Figure 2). Two-thirds of the ARs (22/34, 64.6%) occurred within first 4 months. However, no statistical

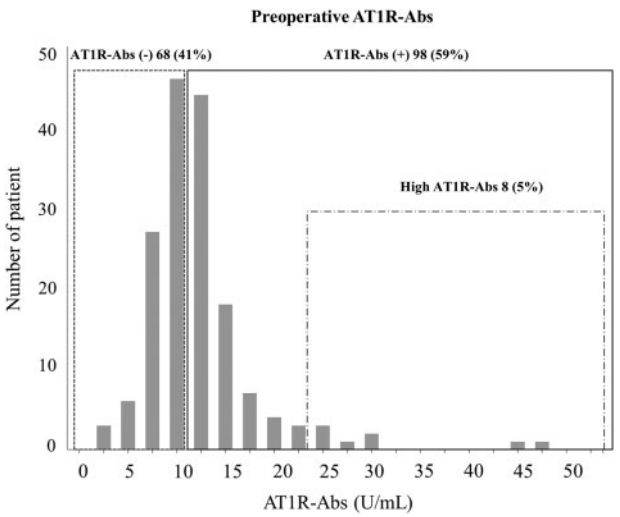

FIGURE 1: Distribution of AT1R-Abs levels. AT1R-Abs, angiotensin II type 1 receptor antibodies.

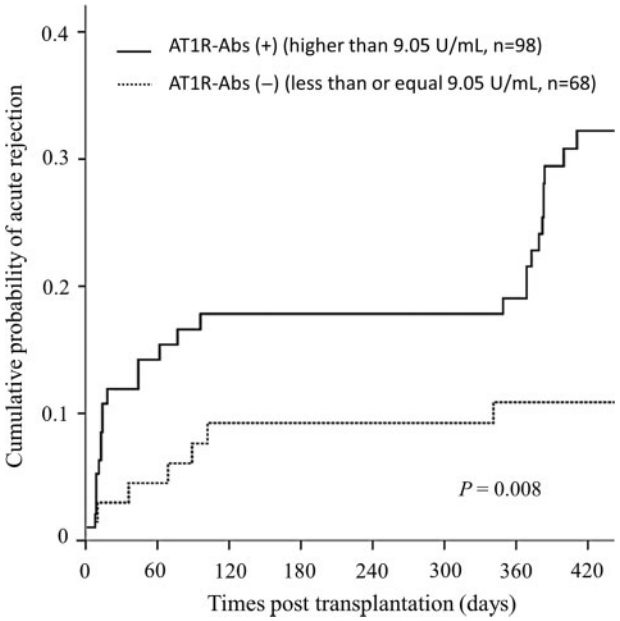

FIGURE 2: Kaplan–Meier analysis of AR episodes in the two groups. AT1R-Abs, angiotensin II type 1 receptor antibodies.

Table 2. Cumulative incidence of AR at time after transplantation

	AT1R-Abs (−) $N = 68$	AT1R-Abs (+) $N = 98$	P-value
Within 1 month	2 (2.9%)	11 (11.2%)	0.054
Within 2 months	3 (4.4%)	13 (13.3%)	0.060
Within 3 months	5 (7.4%)	15 (15.3%)	0.119
Within 4 months	6 (8.8%)	16 (16.3%)	0.153

AT1R-Abs, angiotensin II type 1 receptor antibodies.

difference was observed between pretransplant AT1R-Abs (+) and AT1R-Abs (−) groups at any time point (Table 2).

Univariate and multivariate analyses (Cox regression analysis) showed that pretransplant AT1R-Abs independently predicted BPAR (Table 3).

Histological features of AR according to pretransplant AT1R-Abs

A total of 143 biopsies were performed during the study period; 34 indication biopsies and 109 protocol biopsies. Forty-eight patients underwent multiple biopsies. During the first year post-transplant 34 of 166 patients (20.5%) had AR episodes. Of the 34 patients with AR, 26 had one episode and 8 had two episodes, totalling 42 AR episodes (Figure 3). The histologic features of AR are shown in Table 4. Subclinical BPAR, which was diagnosed by protocol biopsy with normal graft function, was more often observed in the AT1R-Abs (+) group, but this was without statistical significance (65.6 versus 30.0%, P = 0.07). Most cases of BPAR in the present study were diagnosed as ACR. One patient in the AT1R-Abs (+) group developed AMR with ACR, but had no DSA. Banff grades were similar in the two study groups.

MI in high titer of AT1R-Abs (>22.7 U/ml)

Five patients had an MI score of ≥2. None of the five had pretransplant DSA and only one had *de novo* DSA at 1 year after transplantation. Four of the five were presensitized to AT1R, and three patients had a high AT1R-Abs titer (>22.7 U/mL). Arbitrary cut-off values for high titer of AT1R-Abs were defined as mean values plus 2 standard deviations of AT1R-Abs.

The incidences of BPAR were not significantly different between subgroups (12.5% in high titer AT1R-Abs versus 28.9% in low titer, P = 0.439). However, a significantly higher incidence of MI ≥2 was reported in high titer of AT1R-Abs patients than in low titer patients (37.5 versus 1.1%, P = 0.001).

Table 3. Risk factors of AR

Factors	Univariate		Multivariate	
	HR (95% CI)	P-value	HR (95% CI)	P-value
Gender	0.95 (0.40, 2.26)	0.90	–	
Age (years)	1.02 (0.98, 1.06)	0.35	–	
Pretransplant AT1R-Abs (+)	3.75 (1.49, 9.42)	0.005	3.23 (1.40, 7.46)	0.006
HLA mismatch ≥5	1.32 (0.53, 3.28)	0.555	–	
Peak PRA class I >0%	1.21 (0.34, 4.30)	0.774	–	
Peak PRA class II >0%	0.13 (0.01, 1.11)	0.062	0.15 (0.02, 1.16)	0.069
Pretransplant DSA	0.83 (0.12, 5.60)	0.846	0.73 (0.17, 3.17)	0.669
ABO incompatibility	0.738 (0.22, 2.50)	0.625	0.79 (0.28, 2.26)	0.658

HR, hazard ratio; AT1R-Abs, angiotensin II type 1 receptor antibodies; HLA, human leukocyte antigen; PRA, panel reactive antibody; DSA, donor-specific anti-HLA antibody.

Hypertension and use of antihypertensive medications

The frequency of hypertension and the use of antihypertensive therapy were analyzed before and 1 year after transplantation. Of the 166 patients, 140 (84.4%) had a history of treated hypertension and 105 (63.3%) were being treated with antihypertensive drugs at 1 year post-transplant. However, hypertension frequencies were similar in the AT1R-Abs (+) and (−) groups [preoperative hypertension: 83.8% in AT1R-Abs (−) versus 84.7% in AT1R-Abs (+), P = 0.879; post-transplant hypertension: 69.1% in AT1R-Abs (−) versus 59.2% in AT1R-Abs (+), P = 0.192]. No significant intergroup difference was observed between rates of prescription of angiotensin converting enzyme inhibitors or angiotensin receptor blockers before [36.7% in AT1R-Abs (+) versus 42.6% in AT1R-Abs (−), P = 0.443] or after transplantation [10.2% in AT1R-Abs (+) versus 10.3% in AT1R-Abs (−), P = 0.985]. No patient developed malignant hypertension.

Renal function, graft survival and patient death

Renal function was assessed using serum creatinine and GFR. Mean serum creatinine in the AT1R-Abs (+) group was significantly higher than in the AT1R-Abs (−) group at 12 months post-transplant (1.27 ± 0.51 versus 1.13 ± 0.34 mg/dL, P = 0.047). Mean GFR in the AT1R-Abs (+) group was lower than in the AT1R-Abs (−) group at 12 months post-transplant, but this was not statistically significant (62.23 ± 19.14 versus

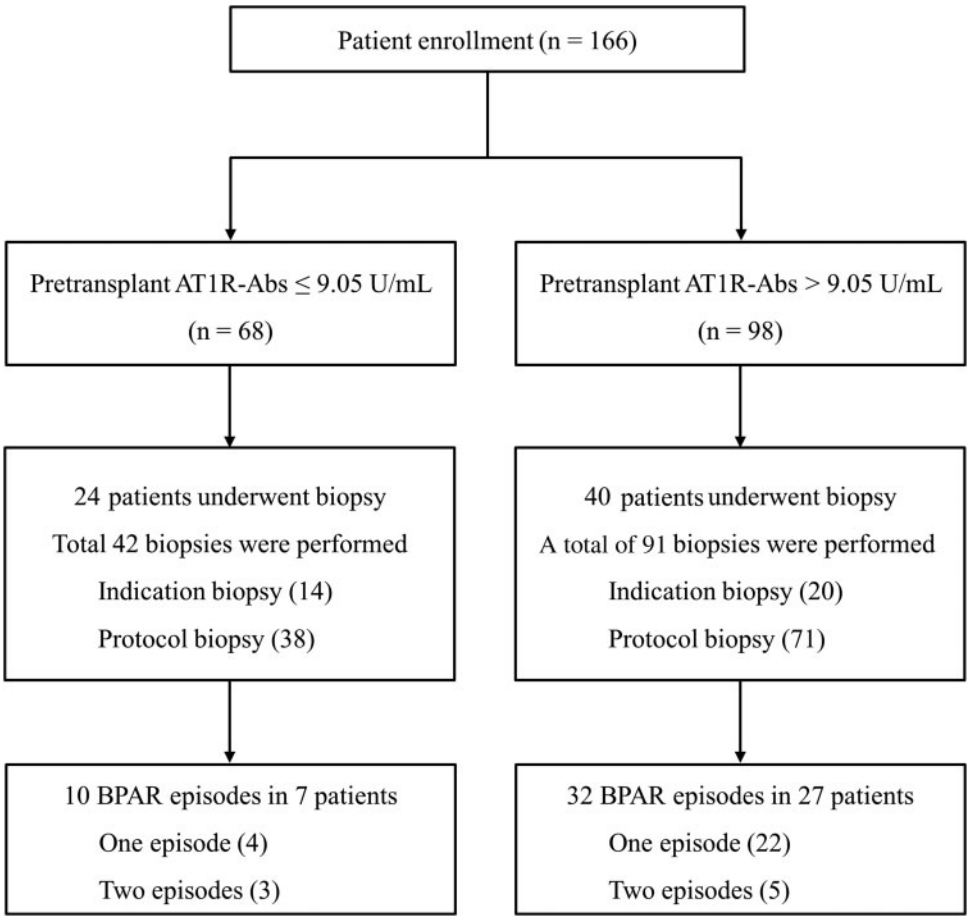

FIGURE 3: BP episodes according to the pretransplant status of AT1R-Abs. AT1R-Abs, angiotensin II type 1 receptor antibodies; BPAR, biopsy-proven acute rejection.

Table 4. Histologic features of graft biopsy in the two groups

	BPAR episodes		
	AT1R-Abs (−) $N = 10$	AT1R-Abs (+) $N = 32$	P-value
Recurrent BPAR	3	5	
Clinical BPAR	7 (70%)	11 (34.4%)	0.07
Subclinical BPAR	3 (30%)	21 (65.6%)	
ACR			
Borderline	5 (50%)	19 (59.4%)	0.79
Grade I	4 (40%)	9 (28.1%)	
Grade II	1 (10%)	4 (12.5%)	
AMR	0	1	

AT1R-Abs, angiotensin II type 1 receptor antibodies; BPAR, biopsy-proven acute rejection; ACR, acute cellular rejection; AMR, antibody-mediated rejection.

65.49 ± 17.10 mL/min/1.73 m^2, P = 0.264). No graft failure or death occurred during the study period.

DISCUSSION

Our study showed that pretransplant AT1R-Abs are associated with development of AR during the first year after transplantation. In addition, recipients with a pretransplant AT1R-Abs level of >9.05 U/mL were found to experience more ARs, independently of traditional immunologic risk factors, such as HLA mismatches, PRA, DSA and ABO incompatibility. Furthermore, our findings suggest a high titer of AT1R-Abs might provoke MIs, indicative of antibody-mediated injury.

Immunological factors play important roles in post-transplant outcomes and graft survival. In recent years, epidemiologic studies have demonstrated that antibody-mediated graft loss is a major cause of graft loss [1, 13, 14]. The detrimental impact of antibodies against HLA on kidney transplantation has been extensively studied. However, the impacts of antibodies against non-HLA antigens are less well understood. Recent studies suggest AT1R-Abs is an independent risk factor of graft failure and AR [7, 8]. However, these studies were conducted over 10 years, and thus, they could have suffered from temporal heterogeneity. In particular, differences in immunosuppression regimens (43.2–48.1% patients used cyclosporine; 34.8–49.4% patients used tacrolimus) in prior studies could have contributed to observed incidences of AR. In addition, ethnic differences in immunogonetic backgrounds might be associated with the prevalence of AT1R-Abs [15].

The cohort of the present study might be considered to have been at relatively low immunologic risk. In fact, only a small percentage of patients had preformed DSA or PRA over 20%. On the other hands, we included ABO incompatible kidney transplant cases (13.3%). This distribution was consistent with the nationwide distribution of Korean transplant cohorts [16].

In this study, the BPAR development rate was higher in the AT1R-Abs (+) group. Interestingly, the majority of patients that developed BPAR were diagnosed as ACR, whereas prior studies focused on AMR. Although the detailed mechanism has not been determined, complementary roles of antibodies in T cell differentiation and cellular immunity could provide a theoretical background for these phenomena. Antibodies and immune complexes function as adjuvants in inducing dendritic cell maturation, thus enhancing their antigen presentation abilities and their secretions of pro-inflammatory cytokines, which lead to the expansion of antigen-specific T cells [17]. A similar tendency has also been observed in HLA-sensitized patients; we previously reported a higher incidence of ACR in sensitized recipients with a positive Luminex crossmatch [18]. Recently, Bagnasco *et al.* reported that ACR occurred more frequently than AMR in recipients that underwent desensitization for preformed DSA [19]. Immune recognition of mismatched HLA results in both cellular and humoral immune mechanisms that lead to allograft rejection. In addition to HLA, some of the antibodies to self-antigens can also induce cellular signals following ligation of their specific antigens [20]. Furthermore, the stimulations of T cells and other immune cells by angiotensin and agonistic antibodies via AT1R increase the productions of pro-inflammatory cytokines [21]. It is evident that such complex immune responses to AT1R might lead to graft injuries.

In the present study, a significantly higher incidence of subclinical BPAR was observed in the AT1R-Abs (+) group. Protocol biopsy timings were determined preoperatively according to the policies of the participating centers, irrespective of AT1R-Abs status. No significant differences were found between Banff scores and rejection severity in the AT1R-Abs (+) and AT1R-Abs (−) groups. In contrast to our results, one prior study concluded that the presence of AT1R-Abs is associated with rejection severity and arteritis [9]. However, the results should be interpreted with caution as only small numbers of patients with severe BPAR ($n = 5$) or arteritis ($n = 4$) were included.

Over the past years, conflicting results have been reported on the effects of rejection severity on clinical outcomes and graft survival [2, 22]. However, recent studies concur that all forms of ACR, regardless of histologic type, including borderline change, can lead to *de novo* DSA formation or chronic AMR [13, 23, 24]. These findings caution that even clinically and histologically mild ACR cases should not be overlooked.

Two-thirds of the ARs occurred within the first 4 months. This finding was consistent with a previous study [7]. We performed further analysis to check the correlation between time and rejection, but no statistical significance was found at any time. Time-dependent analysis findings should be interpreted cautiously, because they might lead to overadjustment. In addition, antibody titer could change after transplantation [7–9].

To evaluate antibody-mediated injury, we investigated MI. Recent studies suggest that MI in glomeruli and peritubular capillaries is probably a more reliable indicator of early injury from circulating DSA than C4d deposition in peritubular capillaries detected in allograft biopsies [25, 26]. In the present study, three patients with a high pretransplant AT1R-Abs titer (>22.7 U/mL) had an MI score of ≥2. Although numbers are small, it may be that elevated AT1R-Abs levels are associated with antibody-mediated damage. We reported results of non-HLA AMR cases with AT1R-Abs that are consistent with this observation [27]. Recently, Fuss *et al.* also reported a consistent association between high titer of AT1R-Abs and AMR [28].

Initial reports of AT1R-Abs-related rejections were accompanied by refractory vascular rejection with malignant hypertension [5]. However, despite the known pathogenic role of AT1R-Abs, these phenotypes were only uncommonly observed in subsequent studies [7, 8]. Furthermore, in the present study, some patients maintained graft function without injury despite the presence of AT1R-Abs. Accordingly, it remains unclear which AT1R-Abs-associated factors (i.e. titer, IgG subclass) affect clinical phenotypes [8].

Although the incidence of AR decreased dramatically after the introduction of more effective immunosuppressive agents, it remains an important risk factor of poor graft outcomes [1, 2]. Thus, determination of the individual risk for BPAR prior to transplantation would have immense clinical value. The current evaluation of the immunologic risk is largely based on the presence of anti-HLA antibodies [29]. However, non-HLA antibodies, especially AT1R-Abs, are also risk factors of AR and graft failure. Consequently, we focused on the pretransplant AT1R-Abs for stratifying immunologic risk. Clinical practice including immunosuppressive strategy and the need for protocol biopsy might be tailored to an individual recipient based on pretransplant AT1R-Abs status. In fact, recent studies have demonstrated that type and amount of immunosuppression (i.e. ATG, rituximab and tacrolimus concentration) could modify clinical outcomes in spite of different immunologic risk [30–32].

The major limitation of this study is its short follow-up. However, most AR events develop in early transplant course and are largely influenced by an individual's alloimmune activity. On the other hand, late onset rejections are mainly influenced by other clinical factors, including non-compliance and *de novo* anti-HLA antibodies [33]. Accordingly, pretransplant AT1R-Abs of the present study might be informative for risk stratification despite the short follow-up. In addition, the study includes heterogeneity across the six centers with respect to indications for biopsy, especially protocol biopsies. Nonetheless, our study is strengthened by its large scale and multicenter Asian cohorts, and it should be noted that few studies have been conducted on AT1R-Abs in Asian populations.

In conclusion, pretransplant AT1R-Abs was found to be an independent risk factor of AR, especially ACR within 1 year of kidney transplantation. In addition, AT1R-Abs titer might be associated with the risk of antibody-mediated injury. Accordingly, pretransplant assessment of AT1R-Abs may be useful for stratifying immunologic risks.

ACKNOWLEDGEMENTS

This work was supported by the Research Program funded by the Korea Centers for Disease Control and Prevention (2012E3301100, 2013E3301600, 2013E3301601#). This work was supported by a faculty research grant of Yonsei University College of Medicine for 2013 (6-2013-0042). The authors thank

the study investigators and coordinators of centers participating in the KNOW-KT study group. The KNOW-KT Study Group includes the following researchers: Curie Ahn, Jaeseok Yang, Jong Cheol Jeong, Seoul National University, Seoul National University Hospital; Yu Seun Kim, Myung Soo Kim, Kyu Ha Huh, Juhan Lee, Yonsei University Health System, Severance Hospital; Sung Joo Kim, Jae Berm Park, Sungkyunkwan University, Seoul Samsung Medical Center; Chan-Duck Kim, Jang-Hee Cho, Hee-Yeon Jung, Kyungpook National University Hospital; Wookyung Chung, Han Ro, Gachon University, Gil Hospital; Sung-Bae Park, Seung-Yeup Han, Eunah Hwang, Wooyeong Park, Keimyung University, Dongsan Medical Center; Byung-Joo Park, Joongyup Lee, Epidemiology and Biostatistics, Department of Preventive Medicine, Seoul National University College of Medicine. Portions of these data were presented at the 2015 American Transplant Congress (ATC) in Philadelphia, PA, USA.

CONFLICT OF INTEREST STATEMENT

None declared.

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Received: 26.7.2015; Editorial decision: 5.10.2015