

CALCULATED PRA AND PIRCHE ALGORITHM IN KIDNEY TRANSPLANT RECIPIENTS

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Abstract

Introduction: Calculated PRA testing in kidney transplantation has revolutionized the field by enabling a more accurate assessment of compatibility and risk prediction for AMR. On the other hand, The PIRCHE algorithm aims to identify the potentially immunogenic human leukocyte antigens (HLA) epitopes on the donor graft that are recognized by the recipient's HLA antibodies.

The aim of this analysis was to compare the actual immunological risk at the time of transplantation with the hypothetical risk that would be determined by cPRA and PIRCHE. Another aim was to compare this hypothetical risk also in the context of the development of DSA and the protocol graft biopsy at month 3.

Material and methods: In a group of 20 patients we recorded the real immunological risk determined at the time of transplantation according to the induction immunosuppression protocol of the Transplant-Nephrology Department of the University Hospital Martin and compared it with the hypothetical calculated risk according to cPRA and PIRCHE. We then compared the hypothetical risk with the protocol biopsy result and with any evidence of donor-specific antibodies at month 3 after the kidney transplantation.

Results: Under cPRA, the two patients we assessed as medium risk in real time would be classified as low risk. Both of these patients did not have DSA identified at month 3 and did not have rejection changes in the protocol biopsy. According to PIRCHE, the immunological risk would change from moderate to low in two patients, and even from very high to low in one patient. In none of these patients did we subsequently observe DSA formation at month 3 post-transplantation, and also all three protocol biopsies were free of rejection changes in these patients.

Conclusion: In our analysis we confirmed the importance of both immunological and non-immunological parameters for determining risk at the time of transplantation. For using PIRCHE score larger studies are required to confirm this strategy.

Key words: kidney transplantation, calculated PRA, PIRCHE, protocol biopsy, donor-specific antibodies

Abbreviations

AMR – antibody-mediated rejection

cPRA – Calculated Panel Reactive Antibody

DSA – donor-specific antibodies

ECD – Expanded Criteria Donor

HLA – Human Leucocyte Antigen

KT – kidney transplantation

MFI – Mean Fluorescent Intensity

PIRCHE – Predicted Indirectly Recognizable HLA Epitopes

SCD – Standard Criteria Donor

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INTRODUCTION

Kidney transplantation is a life-saving treatment option for individuals with an end-stage kidney disease. However, the success of a transplant relies on several critical factors, including the compatibility between the donor and the recipient. One crucial aspect in determining this compatibility is the assessment of the recipient's calculated Panel Reactive Antibody (cPRA) level. The cPRA testing plays a pivotal role in evaluating the risk of antibody-mediated rejection (AMR) and ensuring an optimal organ matching, thus increasing the chances of graft survival post-transplantation. Traditionally, cross-matching tests were used to determine HLA compatibility between the donor and the recipient. However, cPRA offers a more comprehensive assessment by quantifying the percentage of potential donors that a recipient may be incompatible with due to pre-existing antibodies (1).

Several studies have emphasized the significance of cPRA testing in kidney transplantation, where cPRA levels above 80% were associated with an increased likelihood of AMR and graft loss (1, 2).

Calculated PRA testing in kidney transplantation has revolutionized the field by enabling a more accurate assessment of compatibility and risk prediction for AMR. The utilization of PRA testing has led to advancements in personalized patient care, expansion of the donor pool for sensitized patients, and improved overall graft survival rates (3).

To improve the accuracy of assessing immune compatibility, a groundbreaking algorithm called PIRCHE (Predicted Indirectly ReCognizable HLA Epitopes) has emerged as a promising tool in kidney transplantation.

The PIRCHE algorithm, developed by Ingo Thiele and colleagues in 2013, aims to identify the potentially immunogenic human leukocyte antigens (HLA) epitopes on the donor graft that are recognized by the recipient's HLA antibodies (4). Unlike traditional approaches that focus solely on HLA-match compatibility, the PIRCHE algorithm takes into account the subtle variations in HLA epitopes and their potential for immune recognition. By considering indirect recognition of HLA epitopes, the PIRCHE algorithm provides a more comprehensive assessment of alloimmunization risk in kidney transplantation.

Several studies have highlighted the significance of the PIRCHE algorithm in improving transplantation outcomes. PIRCHE scores significantly correlated with the development of de novo donor-specific antibodies (DSA) and the occurrence of AMR (5, 6).

The aim of this analysis was to compare the determined immunological risk according to the standard protocol of the Transplant-Nephrology Department of the University Hospital Martin and the risk that would be determined by cPRA and PIRCHE. Another aim was to compare the result of the protocol biopsy at month 3 after the transplantation (including the determination of the presence of donor-specific antibodies) in the context of cPRA and PIRCHE at the time of the transplantation.

MATERIAL AND METHODS

Patients who underwent transplantation of kidney from a donor after brain death at the Transplant Centre of the University Hospital Martin in 2022 and 2023 were included in the retrospective analysis. All included patients underwent protocol graft biopsy and donor-specific antibody testing. Both protocol biopsy and DSA determination were performed at month 3 after the kidney transplantation, and histological findings were assessed according to the Banff classification 2019. The determination of donor-specific antibodies was performed before the kidney transplantation and in the 3rd month for all patients included in the study by means of the LUMINEX methodology (positivity was stipulated at ≥ 500 MFI). Before the transplantation, anti HLA antibody screening (class I, class II, and MICA) was performed every 3 months by Luminex method and in case of a positive screening, the spe-

cification was also completed. Subsequently, during the kidney allocation itself, we evaluated any DSA positivity.

We retrospectively evaluated immunological risk in all included patients according to a valid immunosuppressive induction protocol as shown in table 1.

Table 1 Induction protocol

	points
PRA > 50% and/or positive DSA	5
PRA 20-50 % and/or positive Luminex screening without DSA	1
Secondary or higher transplantation	5
Positive cross match in history	5
Expected delayed graft function and/or cold ischemia time > 18 hours	1
Dialysis programme > 24 months	1
Expanded criteria donor	1

Induction	points
Anti-thymocyte globulin 6 mg/kg (cumulative dose D0-D6 or as tolerated)	5 and more
Thymoglobulin 3.5 mg/kg cumulative dose D0-D2)	1–4
Basiliximab (D0 and D4)	0

The maintenance immunosuppression consisted of tacrolimus and mycophenolic acid (1080 mg daily dose until the 2nd week after the transplantation, followed by a 720 mg daily dose). Methylprednisolone 500 mg i.v. was administered on day 0 and day 1, followed by the administration of Prednisone 20 mg until the 2nd week after the transplantation, Prednisone 15 mg until the 4th week after the transplantation, Prednisone 10 mg until the 12th week after the transplantation, and Prednisone 7.5 mg until the 12th month after the transplantation, with Prednisone 5 mg administered daily thereafter.

A donor with extended criteria (ECD) means a donor per the definition of ECD codified in 2002: donors over the age of 60 years without co-morbidities or donors over the age of 50 years with at least two co-morbidities that include: blood hypertension, death from cerebrovascular accident, or terminal serum creatinine levels >1.5 mg/dL.

Delayed graft function was defined as the need for dialysis during the first week after the transplantation.

As a next step, we retrospectively performed cPRA and PIRCHE calculations in all patients included in the analysis at the time of the kidney transplantation. According to these values, we then compared the immunological risk that was determined at the real time of the kidney transplantation according to the induction protocol and the hypothetical risk that would have been attributable to the patients according to cPRA or PIRCHE.

The cPRA was determined at the time of the kidney transplantation using a virtual calculator to determine the profile of the panel of reactive antibodies (cPRA), (<https://www.etril>

org/InformationVPRA.aspx), found in the patient's serum. The virtual PRA calculator is a web-based application determining the non-acceptable HLA antigens: HLA-A, -B, -C, -DRB1, -DRB3/4/5, -DQB1, -DQA1, DPB1, and -DPA1. The unacceptable HLA antigens were entered into the virtual PRA calculator based on anti-HLA antibodies detected in the patient's serum using the Luminex method, single-antigen bead class I (SAB1), and single-antigen bead class II (SAB2) (One Lambda/ThermoFisher). Anti-HLA antibodies in each patient's serum were determined individually on the basis of MFI values and cut-off boundaries, and on the basis of the common and specific eplets (<https://www.epregistry.com.br/>) to which anti-HLA antibodies in the Luminex assay bound to each HLA allele. After the determination of unacceptable HLA antigens, we then calculated cPRA (<https://www.etr1.org/vPRA.aspx>) % values for individual patients.

PIRCHE score was determined at the time of the kidney transplantation using the PIRCHE-II algorithm and netMHCIIpan-3.0_IMGT-3.47 database (<https://www.pirche.com/>). Incompatibilities in HLA alleles between the donor and the recipient were determined at the low-resolution level using LinkSeq Real-Time PCR HLA typing (One Lambda/ThermoFisher). HLA typing of the donor and the patient at the low-resolution level: HLA-A, -B, -DRB1, and -DQB1 were imported into the PIRCHE-II algorithm with unique identifiers that paired HLA typing, the patient, and the donor. For all incompatible HLA alleles between the donor and the recipient, we determined the number of peptides derivatized from incompatible HLA alleles of the donor and presented by HLA-DRB1 alleles of the recipient to CD4+ T-lymphocytes of the recipient (PIRCHE-II). Based on PIRCHE-II scores and derived peptides, we determined the immunological risk of predicting the initial de novo formation of de novo DSA and anti-HLA antibodies against individual peptides of the HLA-A, -B, -DRB1, and -DQB1 donor alleles.

Ethical approval and consent to participate

All procedures involving human participants have been approved according to the ethical standards of the institutional research committee, including the 1964 Helsinki Declaration and its later amendments of comparable ethical standards.

The clinical and research activities being reported are consistent with the Principles of the Declaration of Istanbul as outlined in the Declaration of Istanbul on Organ Trafficking and Transplant Tourism. No organs were obtained from prisoners and organs were obtained via National – Slovak transplant organization.

Informed consent was obtained from all individual participants included in the study. Patients signed informed consent regarding publishing their data.

Availability of data and material

Informed consent for included participants was checked and approved by the University hospital's ethical committee and all signed informed consents have been archived for at least 20 years after the research was completed.

The datasets analysed during the current study are available in the Transplant Centre Martin in University hospital Martin in the central repository and in the Hospital Central medical information system (MEDEA). The datasets analysed during the current study are available from the corresponding author on reasonable request.

RESULTS

Twenty patients were included in the cohort, with only one patient undergoing a secondary kidney transplantation. In a first step, the cohort was divided according to the standard immunological risk resulting from the induction immunosuppression protocol (as shown in table 1), resulting in 3 groups – low immunological risk (green), intermediate (orange), and high (red) – figure 1.

initials	risk	waiting time (days)	dialysis program (months)	mismatch	Luminex WL	PRA (%)	number of KT
MH	1	43	15	1-1-2	negative	0/0	1
DK	1	363	11	1-1-1	negative	2/2	1
PH	1	14	1	0	negative	0/0	1
AZ	1	207	25	1-1-1	negative	2/2	1
JŠ	1	34	6	1-1-1	negative	0/0	1
MB	1	29	8	1-1-1	negative	0/0	1
MP	1	20	23	1-1-1	negative	0/0	1
VČ	1	130	10	2-2-0	negative	0/0	1
SK	2	203	12	2-2-1	II. class positive (14872 MFI), no DSA	0/0	1
KS	2	952	42	2-1-0	negative	0/0	1
JB	2	261	23	1-1-2	I. class positive (800 MFI), no DSA	1/1	1
MB	2	297	63	1-1-1	negative	0/0	1
AT	2	1189	86	0	negative	1/1	1
RK	2	210	17	1-1-1	I. class posit (MFI 819.87); II. class posit (MFI 614.56); MICA posit, no DSA	0/0	1
RJ	2	431	33	2-2-2	negative	2/15	1
ŠH	2	70	79	1-2-2	negative	2/2	1
VK	2	587	47	1-2-2	negative	5/12	1
EČ	2	455	55	2-1-1	negative	0/0	1
MH	3	157	21	1-2-0	II. class posit (20 000 MFI), MICA posit, no DSA	5/5	2
VG	3	222	21	1-1-2	posit. DSA A2 12000 MFI	2/2	1

Fig. 1 Immunological risk determined according to the induction immunosuppression protocol

initials	risk	waiting time (days)	dialysis program (months)	Mismatch	Luminex WL	PRA (%)	number of KT
KS	1	952	42	2-1-0	negative	2/2	1
MH	1	43	15	1-1-2	negative	0/0	1
DK	1	363	11	1-1-1	negative	2/2	1
MB ↓	1	297	63	1-1-1	negative	0/0	1
AT ↓	1	1189	86	0	negative	1/1	1
PH	1	14	1	0	negative	0/0	1
AZ	1	207	25	1-1-1	negative	2/2	1
JŠ	1	34	6	1-1-1	negative	0/0	1
ŠH ↓	1	70	79	1-2-2	negative	2/2	1
MB	1	29	8	1-1-1	negative	0/0	1
EČ ↓	1	455	55	2-1-1	negative	0/0	1
MP	1	20	23	1-1-1	negative	0/0	1
VČ	1	130	10	2-2-0	negative	0/0	1
SK	2	203	12	2-2-1	II. class positive (14872 MFI), no DSA	0/0	1
JB	2	261	23	1-1-2	I. class positive (800 MFI), no DSA	1/1	1
RK	2	210	17	1-1-1	I. class positive (MFI 819); II. class positive (MFI 614); MICA posit., no DSA	0/0	1
RJ	2	431	33	2-2-2	negative	2/15	1
VK	2	587	47	1-2-2	negative	5/12	1
VG	3	222	21	1-1-2	posit. DSA A2 12000 MFI	2/2	1
MH	3	157	21	1-2-0	II. class posit (20 000 MFI), MICA posit, no DSA	5/5	2

Fig. 2 Immunological risk determined only by immunological factors included in the induction immunosuppression protocol

According to the induction protocol, 8 patients were low risk, 2 patients were high risk, and the remaining patients were classified as intermediate immunologic risk. We proceeded with the hypothesis of using only immunological factors to determine risk (thus only PRA value, Luminex, positive cross match in history, and secondary or higher KT were taken into account). In this case, the risk distribution would change as follows (figure 2): the patients at high risk remained unchanged, but there was a reduction in risk from intermediate to low in 4 patients.

Analogously, we created a hypothesis of risk determination with only non-immunological criteria, where neither patient was at a high immunological risk (figure 3); on the contrary, both patients who were at a very high risk according to immunological factors were in the green and thus at low risk in this case.

We further advanced our hypotheses by including cPRA in the immunological risk assessment (figure 4 – Immunological risk determined by cPRA). According to cPRA, the two patients we assessed as intermediate risk in real time would be classified as low risk. Both of these patients did not have DSA identified at month 3 and did not have rejection changes in the protocol biopsy.

Finally, we evaluated the hypothetical immunological risk based on PIRCHE, figure 5. In this case, two patients would have their immunological risk changed from moderate to low, one patient even from very high to low. In none of these patients did we subsequently observe DSA formation at month 3 post-transplantation and also all three protocol biopsies were free of rejection changes in these patients. Interestingly, a patient who was assessed as high risk according to the standard induction protocol (based on secondary kidney transplantation) would have had a low immunological risk according to PIRCHE, and, as mentioned above, even in this patient there was no evidence of DSAs at month 3 post-transplantation and the protocol biopsies were free of rejection findings. Conversely, up to 5 patients would have been classified from low or intermediate risk to high risk in the PIRCHE risk assessment. We did not observe any rejection changes in the protocol biopsy in these patients; also, there were no confirmed DSAs in these patients at month 3.

The patient who developed DSA at month 3 and also had a positive finding in terms of rejection changes in the protocol biopsy was classified as highest risk according to PIRCHE.

Finally, we compared the PIRCHE value in patients with negative versus positive Luminex while on the waiting list (WL) and also 3 months after the transplantation (table 2). We observed only numerically higher PIRCHE values in patients with positive Luminex examination versus negative patients, without statistical significance.

Initials	risk	waiting time (days)	dialysis program (months)	mismatch	Luminex WL	PRA (%)	number of KT
MH	1	43	15	1-1-2	negative	0/0	1
SK ↓	1	203	12	2-2-1	II. class posit. (14872 MFI), no DSA	0/0	1
DK	1	363	11	1-1-1	negative	2/2	1
JB ↓	1	261	23	1-1-2	I. class posit. (800 MFI), no DSA	1/1	1
PH	1	14	1	0	negative	0/0	1
AZ	1	207	25	1-1-1	negative	2/2	1
JS	1	34	6	1-1-1	negative	0/0	1
RK ↓	1	210	17	1-1-1	I. class posit. (MFI 819); II. class posit. (MFI 614); MICa posit., no DSA	0/0	1
MH ↓ ↓	1	157	21	1-2-0	II. class posit. (20 000 MFI), MICa posit., no DSA	5/5	2
MB	1	29	8	1-1-1	negative	0/0	1
MP	1	20	23	1-1-1	negative	0/0	1
VG ↓ ↓	1	222	21	1-1-2	posit. DSA A2 12000 MFI	2/2	1
VČ	1	130	10	2-2-0	negative	0/0	1
KS	2	952	42	2-1-0	negative	2/2	1
MB	2	297	63	1-1-1	negative	0/0	1
AT	2	1189	86	0	negative	1/1	1
RJ	2	431	33	2-2-2	negative	2/15	1
ŠH	2	70	79	1-2-2	negative	2/2	1
VK	2	587	47	1-2-2	negative	5/12	1
EC	2	455	55	2-1-1	negative	0/0	1

Fig. 3 Immunological risk determined only by non-immunological factors included in the induction immunosuppression protocol

A	Luminex WL negative	Luminex WL positive	P hodnota	B	Luminex 3M negative	Luminex 3M positive	P hodnota
PIRCHE	93,8 ± 48,3	127,4 ± 61,2	0,2775	PIRCHE	104,2 ± 52,3	125,7 ± 58,3	0,5166
A	23,1 ± 14,3	23 ± 15	0,9904	A	24,5 ± 10,8	28 ± 13,9	0,6352
B	18,4 ± 12,8	22 ± 10,4	0,6021	B	15,3 ± 11,6	19,5 ± 8,5	0,4907
DRB	16 ± 13	18,4 ± 13,8	0,7544	DRB	17,5 ± 14,9	17,2 ± 14,2	0,9722
DQB	21,3 ± 15,7	34,2 ± 25,9	0,2631	DQB	31,8 ± 22,5	38,3 ± 18,4	0,5959

Table 2 Comparison of patients with positive and negative Luminex test results
A: waiting list (WL) B: 3 months (M) after kidney transplantation

initials	risk	waiting time (days)	dialysis program (months)	mismatch	Luminex WL	PRA (%)	number of KT	cPRA	DGF	Luminex 3M	protocol biopsy
MH	1	43	15	1-1-2	negative	0/0	1	0	0	negative	no rejection
SK ↓	1	203	12	2-2-1	II. class posit. (14872 MFI), no DSA	0/0	1	0	0	negative	no rejection
DK	1	363	11	1-1-1	negative	2/2	1	0	0	I. class posit. (846MFI), no DSA	no rejection
PH	1	14	1	0	negative	0/0	1	0	0	I. and II. class posit., no DSA, MICa posit	no rejection
AZ	1	207	25	1-1-1	negative	2/2	1	0	0	negative	no rejection
JŠ	1	34	6	1-1-1	negative	0/0	1	0	0	negative	TCMR IA
RK ↓	1	210	17	1-1-1	I. class posit. (MFI 819); II. class posit. (MFI 614); MICa posit., no DSA	0/0	1	0	0	I. and II. class posit. (no DSA), MICa posit.	no rejection
MB	1	29	8	1-1-1	negative	0/0	1	0	1	I. class negative, II. class posit., no DSA	no rejection
MP	1	20	13	1-1-1	negative	0/0	1	0	0	negative	no rejection
VČ	1	130	20	2-2-0	negative	0/0	1	0	0	negative	no rejection
RJ	2	431	33	2-2-2	negative	2/15	1	0	0	negative	no rejection
ŠH	2	70	79	1-2-2	negative	2/2	1	0	0	negative	no rejection
VK	2	587	47	1-2-2	negative	5/12	1	0	0	negative	no rejection
EČ	2	455	55	2-1-1	negative	0/0	1	0	0	negative	no rejection
KS	2	952	42	2-1-0	negative	2/2	1	0	0	negative	no rejection
JB	2	261	23	1-1-2	I. class posit. (800 MFI), no DSA	1/1	1	1	0	negative	no rejection
MB	2	297	63	1-1-1	negative	0/0	1	0	0	negative	no rejection
AT	2	1189	86	0	negative	1/1	1	0	1	I. class posit., no DSA	no rejection
VG	3	222	21	1-1-2	posit. DSA A2 12000 MFI	2/2	1	42	0	I. class posit., no DSA, II. class posit. DSA DQ 22000 MFI	TCMR, ABMR
MH	3	157	21	1-2-0	II. class posit. (20 000 MFI), MICa posit., no DSA	5/5	2	87	0	negative	no rejection

Fig. 4 Immunological risk determined by cPRA

initials	risk	Luminex WL	PRA	number of KT	cPRA	PIRCHE	A	B	DRB	DQB	DGF	Luminex 3rd month after KT	protocol biopsy
MP	1	negative	0/0	1	0	45	6	22	9	0	0	negative	no rejection
KS ↓	1	negative	2/2	1	0	46	24	10	0	0	0	negative	no rejection
DK	1	negative	2/2	1	0	62	11	12	5	15	0	I. class posit. (846MFI), no DSA	no rejection
JŠ	1	negative	0/0	1	0	62	12	3	4	26	0	negative	TCMR IA
MB	1	negative	0/0	1	0	67	19	15	18	11	0	negative	no rejection
MH ↓	1	II. triéda posit. (20 000 MFI), posit. MICa, no DSA	5/5	2	87	71	1	30	1	0	0	negative	no rejection
PH	1	negative	0/0	1	0	72	11	14	10	26	0	I. and II. Class posit., no DSA, MICa posit	no rejection
EČ ↓	1	negative	0/0	1	0	74	16	2	13	24	0	negative	no rejection
VČ	1	negative	0/0	1	0	82	18	21	11	5	0	negative	no rejection
MB	2	negative	0/0	1	0	111	42	20	2	32	1	I. class negative, II. class posit., no DSA	no rejection
JB	2	I. class posit. (800 MFI)	1/1	1	1	117	18	23	32	28	0	negative	no rejection
ŠH	2	negative	2/2	1	0	120	21	27	20	32	0	negative	no rejection
SK	2	II. class posit. (14872 MFI), no DSA	0/0	1	0	78	24	10	9	23	0	negative	no rejection
MH ↑	3	negative	0/0	1	0	136	25	11	26	65	0	negative	no rejection
AT ↑	3	negative	1/1	1	0	138	32	24	36	37	1	I. class posit., no DSA	no rejection
VK ↑	3	negative	5/12	1	0	145	47	28	31	35	0	I. class posit., no DSA	no rejection
VG	3	posit. DSA A2 12000 MFI	2/2	1	42	150	31	13	18	63	0	I. class posit., no DSA, II. class posit. DSA DQ 22000 MFI	TCMR, ABMR
RJ ↑	3	negative	2/15	1	0	180	42	42	30	39	0	negative	no rejection
AZ ↑	3	negative	2/2	1	0	186	44	35	34	49	0	negative	no rejection
RK ↑	3	I. class posit (MFI 819, 87); II. class posit (MFI 614, 56); MICa posit, no DSA	0/0	1	0	221	41	34	32	57	0	I. and II. class posit. (no DSA), MICa posit.	no rejection

Fig. 5 Immunological risk determined by PIRCHE

DISCUSSION

In our analysis, we confirmed the importance of both immunological and non-immunological parameters for determining the risk at the time of the transplantation. Comparing our determined immunological risk at the time of the transplantation (according to the valid induction immunological risk) and immunological risk according to cPRA and PIRCHE, respectively, we identified patients in whom the determined risk did not match. Nevertheless, although their "new" immunological risk according to cPRA or PIRCHE was assessed to be lower compared to the actual established risk, we did not find any evidence of rejection changes or DSA in these patients at month 3 post-transplantation. This can be mainly explained by the fact that there was only one patient with a high cPRA value in the whole cohort. It is in patients with a cPRA value of more than 85 and 95%, respectively, that such an immunological risk assessment is warranted. Understanding a recipient's PRA level allows transplant professionals to identify potential mismatched donors and develop strategies to mitigate the risk of AMR. Advanced techniques such as virtual cross-matching and desensitization protocols have emerged as effective tools for improving transplantation outcomes in patients with higher PRA levels. Virtual cross-matching uses a combination of PRA results and donor-specific antibody (DSA) testing to predict the risk of AMR, assisting in donor selection, and promoting better graft survival rates. Moreover, desensitization procedures involving therapeutic interventions such as plasmapheresis, intravenous immunoglobulin administration, and rituximab have shown promising results in reducing PRA levels, thereby expanding the pool of compatible donors for highly sensitized patients (3).

When we evaluated PIRCHE in the context of positive and negative results of Luminex examination in the studied patients, we did not confirm a significant difference (numerical only). However, we know that the high immunological risk evaluated by the PIRCHE algorithm is mainly indicative of DSA formation in the long term. A study by Spitznagel et al. confirmed in 123 patients that a high PIRCHE score (median 101.50 vs. 74.00) predicted TCMR changes (6).

Specific HLA-antigen disparities can trigger considerable clinical alloreactivity and are classified as notably immunogenic HLA mismatches. Conversely, certain HLA-antigen mismatches typically do not result in clinical alloreactivity. This underscores the importance of pinpointing molecular HLA-epitope mismatch rather than solely relying on the number of HLA-antigen mismatches. The PIRCHE algorithm emerges as a more suitable tool for stratifying the risk of immune-mediated injury. Geneugelijk et al. documented in 2018 a robust association between higher PIRCHE-II scores and an elevated risk of kidney allograft failure (7, 8). Furthermore, based on their multivariate analysis, the prognostic value of PIRCHE-II scores exceeded that of HLA-antigen mismatches. Studies have demonstrated that the predictive prowess of PIRCHE-II scores in predicting de novo DSA development is most pronounced for HLA-DQ and HLA-DR, followed by HLA-A and HLA-B (9, 10, 11, 12).

The implementation of the PIRCHE algorithm in clinical practice holds several advantages. Firstly, it provides a more precise assessment of immune compatibility, allowing physicians to make informed decisions regarding donor selection and risk stratification. Moreover, the algorithm can guide personalized immunosuppressive strategies to prevent and manage alloimmune responses, ultimately improving graft survival rates. PIRCHE algorithm represents a significant advancement in assessing alloimmunity and improving kidney transplantation outcomes. By evaluating the compatibility of HLA epitopes and their potential immunogenicity, this algorithm provides a better understanding of the risks associated with graft rejection. As the field of kidney transplantation continues to evolve, the integration of the PIRCHE algorithm into clinical practice has the potential to enhance personalized patient care and optimize long-term transplant success (13, 14).

CONCLUSION

In conclusion, calculated PRA testing in kidney transplantation has revolutionized the field by enabling a more accurate assessment of compatibility and risk prediction for ABMR. The utilization of PRA testing has led to advancements in personalized patient care, expansion of the donor pool for sensitized patients, and improved overall graft survival rates (15).

The utilization of PIRCHE for organ allocation has been documented in small studies involving uniform populations. Larger studies are required to confirm this strategy. Challenges in employing this method of epitope matching for donor selection involve the need for clearer differentiation between eplet-mismatch load and immunogenic eplets, as well as the availability of analysis software (8, 16).

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