Clinical Kidney Journal, 2023, vol. 16, no. 11, 2226–2234

https://doi.org/10.1093/ckj/sfad124
Advance Access Publication Date: 15 June 2023
Original Article

ORIGINAL ARTICLE

Association between Kidney Donor Risk Index, kidney graft function and histological changes in early post-transplant graft biopsy

Natalia Słabiak-Błaż, Agata Kujawa-Szewieczek, Aureliusz Kolonko, Joanna Ziółkowska, Henryk Karkoszka, Andrzej Więcek and Grzegorz Piecha

Department of Nephrology, Transplantation and Internal Medicine, Medical University of Silesia, Katowice, Poland

Correspondence to: Grzegorz Piecha; E-mail: g.piecha@outlook.com

ABSTRACT

Background. Proper assessment of donor organ quality is crucial for optimal kidney allocation and best long-term outcomes. The aim of this study was to analyze the association between the Kidney Donor Risk Index (KDRI) and histological parameters in early post-transplant graft biopsy in a Polish cohort of kidney transplant recipients.
Methods. In 418 consecutive kidney transplant recipients, a histological evaluation of very early [at median 11 (9–13) post-transplant day] protocol core needle biopsy was performed and analyzed according to the Banff classification. Subjects were divided into quartiles of the KDRI value. Kidney graft function, patient and graft survival were also analyzed over a median follow-up period of 44 (26–56) months.
Results. There was a significant trend toward greater intensity of chronic histology changes along the KDRI quartiles ($\chi^2 = 20.8$; $P < .001$), including interstitial fibrosis, tubular atrophy, mesangial matrix increase and arteriolar hyalinosis. Stepwise multivariate regression analysis revealed that only higher KDRI value independently increased the severity of chronic graft injury ($r_{partial} = 0.340$, $P < .001$). KDRI values were valuable in the determination of both early and long-term graft function.
Conclusion. The KDRI values correlate with chronic histological changes found in early post-implantation kidney biopsies and can also be helpful in the prediction of graft outcome.

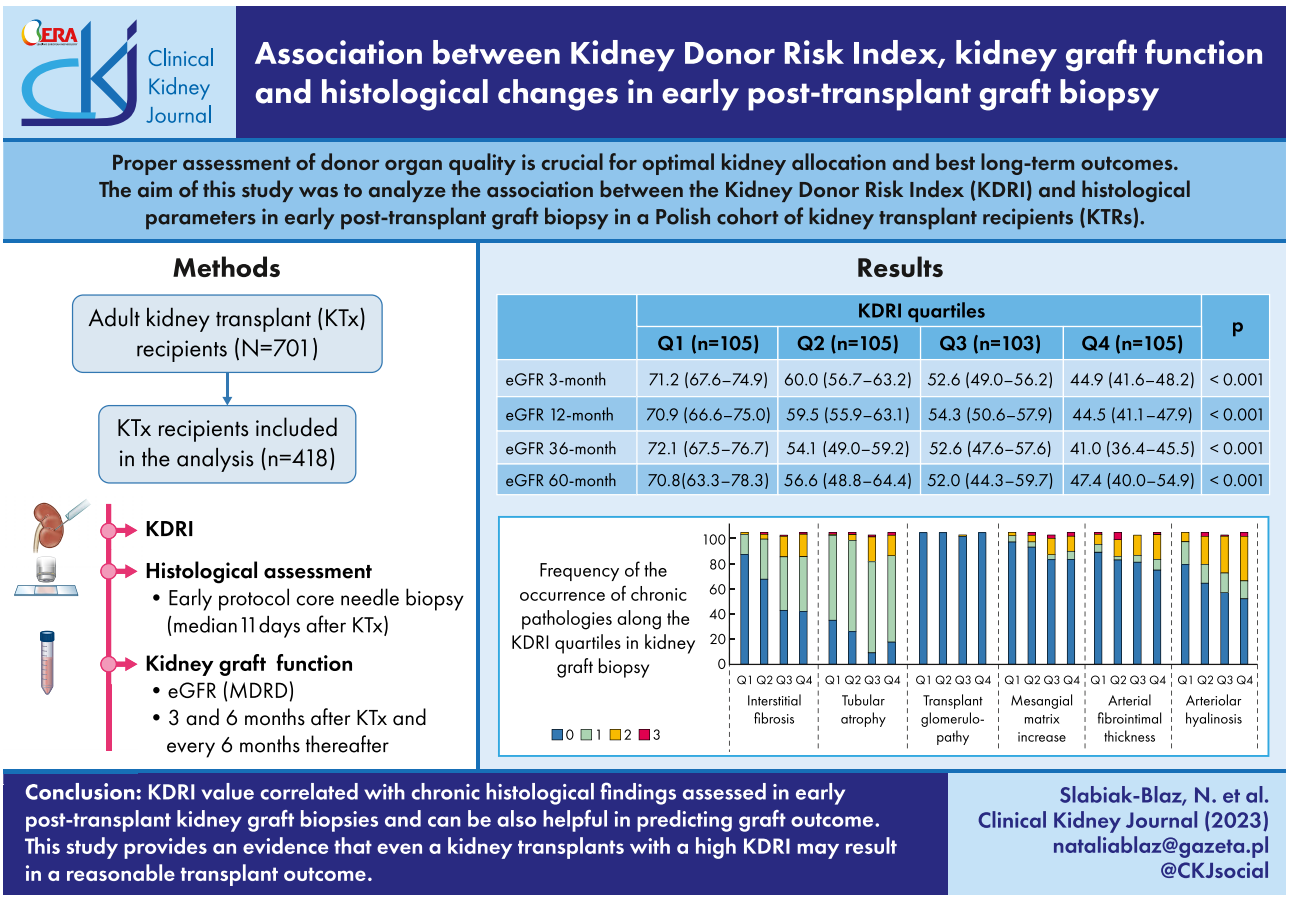
LAY SUMMARY

We investigated an association between the Kidney Donor Risk Index (KDRI; based on donor demographics, medical history and factors related to donor death) and histological parameters in early post-transplant kidney graft biopsy. In 418 consecutive kidney transplant recipients, a histological evaluation of protocol core needle biopsy was performed and analyzed according to the Banff classification. More intense chronic histology changes including interstitial fibrosis, tubular atrophy, mesangial matrix increase and arteriolar hyalinosis were observed with increasing KDRI. Over 5 years of observation, post-transplant better kidney function (measured as higher estimated glomerular filtration rate) was observed with lower KDRI. There was no significant difference in the rate of early

Received: 10.12.2022; Editorial decision: 9.5.2023

surgical complications, acute rejection episodes or the need for hospitalization due to a serious infection. Stepwise multivariate regression analysis revealed that only higher KDRI value independently increased the severity of chronic graft injury.

GRAPHICAL ABSTRACT



Keywords: early post-transplant biopsy, graft outcome, kidney allocation, Kidney Donor Risk Index, kidney transplantation

INTRODUCTION

Kidney transplantation is the optimal treatment for patients with end-stage renal disease [1] and post-transplant care ensures optimal patient and graft survival [2]. However, due to the permanent organ shortage a substantial proportion of organs is procured from extended criteria donors (ECD) [3]. The long-term outcomes of ECD kidney transplants are significantly worse than those of standard criteria donors, but nevertheless better than non-transplanted patients on chronic dialysis [4, 5]. In the effort to optimize the results of kidney transplantation programs, different approaches have been proposed for the pre-transplant assessment of organ quality, including pre-implantation biopsy with histologic scoring [6], ECD definition introduced in 2002 [3], machine perfusion with perfusate analysis or perfusion dynamics measurement, or several clinical scores [7].

The Kidney Donor Risk Index (KDRI) has gained a growing interest. It consists of 10 donor variables, including demographics, medical history and factors related to donor death, and was invented in order to quantify the risk of organ failure during the long-term post-transplant observation [8]. Several studies from the USA showed that higher KDRI values are associated with shorter half-life of kidney transplants and that KDRI is an accurate predictor of donor contributions to transplant outcomes [8, 9]. Therefore, since 2014 it has been used in a new US kidney allocation system to improve donor–recipient matching and to maximize the potential survival of every transplanted kidney [10].

The KDRI system has not been implemented in the allocation system in Europe; however, information from recent studies may suggest its usefulness also in the European population. The German study by Lehner *et al.* [11] showed that the Kidney Donor Profile Index (KDPI; which maps the KDRI, a measure of relative risk, to a cumulative percentage scale) also predicted graft survival in the European population leading to worse performance as KDRI increases. The use of KDRI in the Polish population has

not yet been well established. A study by Serwanska-Swietek *et al.* [12] showed that graft function as assessed by estimated glomerular filtration rate (eGFR) after 1 year in ECD recipients was significantly different according to KDRI scores, with lower KDRI values corresponding with better outcomes. This study suggests that KDRI may facilitate the improvement of the kidney allocation system in Poland as well, but further research with a longer follow-up period is needed.

The second goal of KDRI introduction was to limit the percentage of discarded kidneys [13]. Nevertheless, in the USA and in some European countries the in-depth quality assessment of marginal kidneys is based mainly on the pre-implantation biopsy [7, 14, 15], the utility of which for predicting transplant outcomes is limited [16, 17]. On the other hand, it has been suggested that chronic histological changes identified in early post-reperfusion biopsies better correlate with graft outcomes [18, 19].

To our knowledge, there are no studies evaluating the correlation of KDRI with chronic histologic abnormalities present in early (within 2 weeks of transplantation) post-reperfusion biopsies in the Polish population. Therefore, this study aimed to assess the usefulness of KDRI in the Polish population by analyzing the relationship between KDRI, histological parameters in early post-transplant biopsy and post-transplant graft function in kidney transplant recipients.

MATERIALS AND METHODS

Study group

This retrospective single-center cohort study included 701 adult patients who successively received a kidney transplantation from January 2015 to June 2021 at the A. Mielecki Hospital of Medical University of Silesia in Katowice, Poland. Living donor recipients ($n = 17$) as well as multiple organs recipients ($n = 21$) were excluded from the study. Among these patients, we identified 418 cadaveric kidney graft recipients who underwent early protocol core needle biopsy. All patients received a triple immunosuppression regimen, including tacrolimus, mycophenolate mofetil and steroids, given as pulse intravenous doses of methylprednisolone followed by an oral prednisone taper.

The primary outcome of the study was the histological evaluation of the kidney transplant based on early post-reperfusion kidney biopsy in relation to donor kidney quality based on KDRI calculations. The secondary objective was to assess graft function assessed by eGFR up to 5 years after transplantation, and early graft function: delayed graft function (DGF), immediate graft function (IGF), slow graft function (SGF), and early and late post-transplant complications according to KDRI quartiles.

Kidney graft biopsy

Informed consent for protocol biopsy was obtained from all kidney graft recipients. The procedure of early protocol graft biopsy was scheduled during the first post-transplant hospitalization in the Department of Nephrology Transplantation and Internal Medicine, Medical University of Silesia in Katowice, Poland at least 8 days after transplant surgery. The primary goal of these protocol biopsies is the diagnostics of subclinical acute rejection. Immediate post-reperfusion biopsies are not routinely performed at our center. All biopsies were reviewed by the same pathologist. Biopsies that were considered as inadequate or lacked scoring of the relevant individual lesions were excluded from the analysis. The severity of individual histological lesions was scored semi-quantitatively according to the latest available International Banff Classification for Allograft Pathology [20–23]. The percentage of sclerotic glomeruli was also evaluated. Finally, the individual histologic findings were grouped as acute inflammatory (interstitial inflammation, tubulitis, glomerulonephritis, arteritis and peri-tubular-capillaritis) or chronic changes (interstitial fibrosis, tubular atrophy, transplant glomerulopathy, matrix growth mesangial, fibrous arterial membrane thickness and arterial hyalinosis).

KDRI and study groups

The KDRI was calculated retrospectively as donor-only KDRI according to the formula proposed by Rao *et al.* [8], using the data from the organ donor reporting card. The KDRI uses 10 donor variables, including elements of donor demographics (age, height, weight, ethnicity), medical history (hypertension, diabetes, hepatitis C status) and factors related to donor death (cause of death, terminal serum creatinine, brain or cardiac death). We calculated KDRI to a reference donor (KDRI = 1.00) corresponding to a 40-year-old, non–African American man, height 1.70 m, weight 80 kg, with a serum creatinine of 1.0 mg/dL, without diabetes, hypertension or a cerebrovascular cause of death, who is hepatitis C virus negative and brain dead. We did not scale the KDRI to a local donor population as this data was not available to us. The study subjects were divided into quartiles (Q) according to the KDRI value. The median KDRI values within quartiles were 0.83 (Q1–Q3: 0.74–0.88) vs 1.07 (1.0–1.15) vs 1.31 (1.25–1.38) vs 1.75 (1.55–1.89) in Q1 vs Q2 vs Q3 vs Q4, respectively.

Patient and graft outcomes

The long-term transplant outcomes were observed until December 2021 (at least 6 months after transplantation). Serum creatinine (S_{Cr}) concentrations were analyzed at post-operative days (POD) 3 and 7, then at the day of discharge from the hospital, 3 and 6 months after transplantation and every 6 months thereafter. IGF was characterized by S_{Cr} <3 mg/dL at POD 3, and SGF as S_{Cr} >3 mg/dL at POD 3. DGF was recognized in patients who required dialysis therapy after transplantation. Based on S_{Cr} values, an eGFR was calculated using the Modification of Diet in Renal Disease formula. Pre- and post-transplant major adverse cardiovascular events (MACE) were defined as myocardial infarct, stroke, or coronal artery by-pass graft or stenting. During the follow-up period, patient and graft survival were analyzed, as well as the frequency of the most common complications, including acute rejection (AR), post-transplant diabetes mellitus (PTDM), infectious and surgical or urological complications (reoperations due to serious bleeding, ureteral or kidney graft artery stenosis or urine leak).

Statistical analysis

Statistical analyses were performed using STATISTICA 13.3 PL for Windows (Tibco Inc., Palo Alto, CA, USA) and MedCalc v19.2.1 (MedCalc Software, Mariakerke, Belgium). Values are presented as means with 95% confidence interval, medians with Q1–Q3 values, or frequencies. The main study comparison was performed between four groups of patients based on the KDRI quartiles, using the ANOVA test (for quantitative variables) or the χ^2 test (for qualitative variables). Variables with non-normal distribution were compared using the Kruskal–Wallis test. The comparisons between particular groups were performed using the Mann–Whitney U test. The statistical significance of trend was verified using the χ^2 test. Correlation analyses were performed using the Spearman rank test. A stepwise multiple regression

Table 1: Clinical characteristics of study subjects.

Parameter	All ($n = 418$)	KDRI quartiles				P
		Q1 ($n = 105$)	Q2 ($n = 105$)	Q3 ($n = 103$)	Q4 ($n = 105$)	
Age[a] (years)	51 (40–60)	44 (37–55)	51 (38–58)	48 (40–58)	60 (50–66)[#]	<.001
Sex (M/F)	262/156	65/40	63/42	61/42	73/32	.40
BMI (kg/m^2)	25.4 (25.1–25.8)	25.1 (24.3–25.9)	25.1 (24.3–25.8)	25.2 (24.5–25.9)	26.4 (25.7–27.1)[*]	<.05
Dialysis vintage[a] (months)	29 (19–46)	31 (16–55)	28 (22–44)	28 (18–47)	29 (20–45)	.99
Residual diuresis[a] (mL/day)	400 (50–1000)	500 (50–1500)	225 (0–1000)	400 (100–1000)	500 (100–1000)	.27
Hypertension, *n* (%)	396 (94.7)	101 (96.2)	97 (92.2)	96 (93.2)	102 (97.1)	.33
Pre-transplant diabetes, *n* (%)	59 (14.1)	9 (8.6)	19 (18.1)	15 (14.6%)	16 (15.2)	.24
Pre-transplant MACE, *n* (%)	59 (14.1)	12 (11.4)	15 (14.3)	7 (6.8)	25 (23.8)	<.01
ESRD cause, *n* (%)						
Glomerulonephritis	173 (41.4)	49 (46.7)	52 (49.5)	38 (36.9)	34 (32.4)[†]	.05
Pyelonephritis	34 (8.1)	12 (11.4)	5 (4.8)	10 (9.7)	7 (6.7)	.42
ADPKD	59 (14.1)	15 (14.3)	14 (13.3)	11 (10.7)	19 (18.1)	.54
Hypertension	50 (12.0)	13 (12.4)	8 (7.6)	9 (8.7)	20 (19.1)[††]	.07
Diabetes mellitus	40 (9.6)	5 (4.8)	14 (13.3)	10 (9.7)	11 (10.5)	.28
Other/unknown	81 (19.4)	17 (16.2)	17 (16.2)	27 (26.2)	20 (19.0)	.20

Data presented as means with 95% confidence interval, [a]medians with Q1–Q3 values, or frequencies.
Statistics: ANOVA, Kruskal–Wallis test or χ^2 test. [*]$P < .05$; [#]$P < .001$ for Q4 vs Q1, Q2 and Q3, [†]$P < .05$ for Q4 vs Q1 and Q2; [††]$P < .05$ for Q4 vs Q2 and Q3.
M, male; F, female; ESRD, end-stage renal disease; ADPKD, autosomal dominant polycystic kidney disease.

Table 2: Transplant characteristics by KDRI quartiles.

Parameter	All ($n = 418$)	KDRI quartiles				P
		Q1 ($n = 105$)	Q2 ($n = 105$)	Q3 ($n = 103$)	Q4 ($n = 105$)	
Retransplant, *n* (%)	70 (16.7)	27 (25.7)[*]	19 (18.1)	12 (11.7)	12 (11.4)	<.05
HLA mismatch class I	2.29 (2.19–2.38)	2.19 (1.99–2.39)	2.23 (2.06–2.40)	2.38 (2.18–2.58)	2.34 (2.15–2.53)	.40
HLA mismatch class II	0.67 (0.61–0.72)	0.59 (0.49–0.69)	0.64 (0.53–0.74)	0.59 (0.48–0.70)	0.84 (0.71–0.96)[#]	<.001
Last PRA >25%, *n* (%)	25 (6.0)	9 (8.6)	8 (7.6)	6 (5.8)	2 (1.9)	.18
CIT (h)	17.3 (16.7–17.9)	17.5 (16.4–18.7)	16.2 (14.9–17.4)	17.5 (16.2–18.7)	18.1 (17.0–19.2)	.15
Induction therapy, *n* (%)						
None	64 (15.3)	25 (23.8)	15 (14.3)	16 (15.5)	8 (7.6)[†]	<.05
Basiliximab	209 (50.0)	43 (41.0)	54 (51.4)	49 (47.6)	63 (60.0)[††]	.07
rATG	160 (38.3)	40 (38.1)	41 (39.0)	40 38.8)	39 (37.1)	.98
Rituximab	3 (0.7)	2 (1.9)	1 (1.0)	0 (0.0)	0 (0.0)	.30

Data presented as medians with Q1–Q3 values, or frequencies.
[*]$P < .05$ for Q1 vs Q3 and Q4; [#]$P < .05$ for Q4 vs Q1, Q2 and Q3; [†]$P < .05$, [††]$P < .01$ for Q4 vs Q1.
PRA, panel reactive antibodies; CIT, cold ischemia time; rATG, rabbit anti-thymocyte globulin.

analyses were performed for the severity of chronic kidney graft injury and the percentage of sclerosed glomeruli as dependent variables. Model I for chronic lesions included recipient's age, re-transplantation, the use of induction therapy and KDRI value as potential independent variables, whereas Model II for the percentage of sclerotic glomeruli included retransplantation, HLA class II mismatch, very early AR episode (diagnosed at the time of biopsy based on the protocol biopsy) and KDRI value. The variables used as potential independent predictors in multivariate analysis were selected based on the significant differences in the clinical characteristics between analyzed KDRI quartiles and subsequent univariate regression. For all analyses, a P-value <.05 was considered statistically significant.

RESULTS

Study group

The clinical characteristics of study subjects divided into four groups based on KDRI values is shown in Table 1. All recipients were Caucasian. Patients in Q4 were significantly older than the rest of study participants, probably as a result of an old-to-old allocation program: the organs procured from donors >65 years of age are offered to the recipients >60 years. In line wth this, also body mass index (BMI) in Q4 was the significantly higher than in the lower quartiles. There was no significant differences in dialysis vintage, residual diuresis and pre-transplant comorbidity between study groups, except for the rate of previous MACE, which was significantly greater in Q4 than in Q1 and Q3.

Most of the study patients (85%) received induction therapy. However, the percentages of overall usage of induction therapy and usage of basiliximab were greater in Q4 (92.4% and 57.1%, respectively) than in Q1 (77.2% and 39%, respectively) (Table 2). There was no difference in polyclonal antibodies (antithymocyte globulin) or incidental rituximab induction between groups. The percentage of retransplants was significantly greater in Q1 than in Q3 and Q4 patients (Table 2), whereas the HLA class II mismatch was the highest in Q4. There was no difference in HLA class I mismatch, cold ischemia time or the percentage of recipients with last pre-transplant PRA titer >25% (Table 2).

Table 3: Early and long-term kidney graft function and post-transplant complications.

Parameter	All ($n = 418$)	KDRI quartiles				P
		Q1 ($n = 105$)	Q2 ($n = 105$)	Q3 ($n = 103$)	Q4 ($n = 105$)	ANOVA for trend
Early graft function						
IGF, *n* (%)	130 (31.1)	57 (54.3)	36 (34.3)	24 (23.3)	13 (12.4)	<.001*, $\chi^2 = 42.7$
SGF, *n* (%)	205 (49.0)	42 (40.0)	49 (46.7)	54 (52.4)	60 (57.1)	<.05*, $\chi^2 = 6.2$
DGF, *n* (%)	103 (24.6)	12 (11.4)	24 (22.9)	29 (28.2)	38 (36.2)	<.001*, $\chi^2 = 17.2$
POD 3 SCr[a] (mg/dL)		3.0 (1.6–6.5)	4.6 (2.5–7.4)	5.8 (3.1–9.4)	6.4 (4.3–9.6)	<.001
POD 7 SCr[a] (mg/dL)		1.5 (1.0–2.9)	1.9 (1.3–5.0)	3.4 (1.6–6.5)	4.8 (1.9–7.6)	<.001
SCr at discharge[a] (mg/dL)		1.2 (0.9–1.6)	1.4 (1.1–2.0)	1.6 (1.3–2.2)	1.9 (1.5–2.7)	<.001
Duration of hospital stay[a] (days)		14 (12–18)††	14 (13–19)††	15 (13–23)†	17.5 (14–28)	<.001
Follow-up eGFR (mL/min/1.73 m^2)						
3-month	54.2 (52.2–56.1)	71.2 (67.6–74.9)	60.0 (56.7–63.2)	52.6 (49.0–56.2)	44.9 (41.6–48.2)	<.001
6-month	54.0 (52.1–56.0)	71.0 (65.9–74.2)	59.5 (56.1–63.0)	53.0 (49.2–56.8)	46.1 (43.0–49.2)	<.001
12-month	54.3 (52.3–56.4)	70.9 (66.6–75.0)	59.5 (55.9–63.1)	54.3 (50.6–57.9)	44.5 (41.1–47.9)	<.001
36-month	54.9 (51.6–58.1)	72.1 (67.5–76.7)	54.1 (49.0–59.2)	52.6 (47.6–57.6)	41.0 (36.4–45.5)	<.001
60-month	53.7 (48.0–59.3)	70.8 (63.3–78.3)	56.6 (48.8–64.4)	52.0 (44.3–59.7)	47.4 (40.0–54.9)	<.001
Complications, *n* (%)						
Surgical complications	40 (9.6)	7 (6.7)	11 (10.5)	6 (5.8)	16 (15.2)	.09
Early AR	69 (16.5)	22 (20.9)	15 (14.3)	13 (12.6)	19 (18.1)	.48
12-month AR	82 (19.6)	23 (21.9)	16 (15.2)	19 (18.5)	24 (22.9)	.49
PTDM	55 (13.2)	18 (17.1)#	8 (7.6)	8 (7.8)	21 (20.0)#	<.05
12-month hospitalization due to infection	107 (25.6)	27 (25.7)	24 (22.9)	25 (24.3)	31 (29.5)	.61
Graft loss	23 (5.5)	2 (1.9)	7 (6.7)	4 (3.9)	10 (9.5)	.08
Death	53 (12.7)	8 (7.6)	12 (11.4)	17 (16.5)	16 (15.2)	.21

Data presented as means with 95% confidence interval, [a]medians with Q1–Q3 values or frequencies.
Statistics: ANOVA, Kruskal–Wallis or χ^2 test; *P for trend; #$P < .05$ vs Q2 and Q3; †$P < .05$, ††$P < .01$, †††$P < .001$ vs Q4.
Early AR—occurring up to 3 months post-transplant.

Early and long-term kidney transplant outcomes

There were no primary graft non-function cases among all study patients. There were significant differences in serum creatinine concentrations during the early post-transplant period, with the lowest values in Q1 and the highest in Q4 group (Table 3). Accordingly to the consecutive KDRI quartiles, we observed a significant decreasing trend for IGF occurrence; instead there was an increasing trend for SGF and DGF occurrence, with their highest rate in Q4 (Table 3). Moreover, a significantly longer hospitalization after transplantation was also noted in Q4 patients vs other study groups.

In the long-term follow-up period, the highest eGFR values were observed in Q1 subjects, and the lowest in the Q4 group (Table 3). At 3-month and 6-month time-points, eGFR values in all four groups differed significantly, at 12-month and 36-month time-points the differences between Q2 and Q3 were no longer significant, and 5 years post-transplantation eGFR in Q1 group was significantly higher than in the remaining three groups. A strong significant correlations were found between KDRI value and eGFR at 3 months (R = 0.515), 6 months (R = 0.466), 12 months (R = 0.493), 36 months (R = 0.529) and 60 months (R = 0.471), all $P < .001$.

There was no significant difference between the groups in the rate of early surgical complications, AR episodes occurring up to 12 months post-transplant or the need for hospitalization due to a serious infection. The significantly greater occurrence of PTDM was noted in Q1 and Q4 vs Q2 and Q3 groups (Table 3).

During a median follow-up period of 44 (26–56) months, which was similar between study groups, there were 55 deaths (13.2%) and 22 graft losses (5.3%) in the whole study group. The most common causes of death were infectious complications (60%), including 18 cases (54.5% of all infection-related deaths) of COVID-19, and cardiovascular complications (20%). There was an increasing trend for the occurrence of a combined end-point (graft loss or death) across KDRI quartiles ($\chi^2 = 9.0$, $P < .01$).

KDRI values and early protocol kidney graft biopsy findings

The early protocol kidney graft biopsies were performed at median 11 (9–13) POD. The median number of glomeruli per biopsy was 23 (15–30). In a whole study group, any inflammatory changes were observed in 65.5% of biopsies (Fig. 1A), including 53.7% of low-scaled findings (1–3 points out of 15-point scale) and 3.4% of intensified pathology (>6 points). There was a weak significant trend toward greater intensity of inflammatory changes along the increasing KDRI quartiles ($\chi^2 = 4.16$; $P < .05$). It is worth noting that only 12.0% of all biopsies were without chronic changes (Fig. 1B). In 57.1% of biopsies we noted the presence of low-scaled chronic changes (1–3 out of 18-point scale), whereas 5.3% of biopsies presented advanced (>6 points) chronic kidney pathology. There was a significant trend toward greater intensity of chronic histology changes along the KDRI

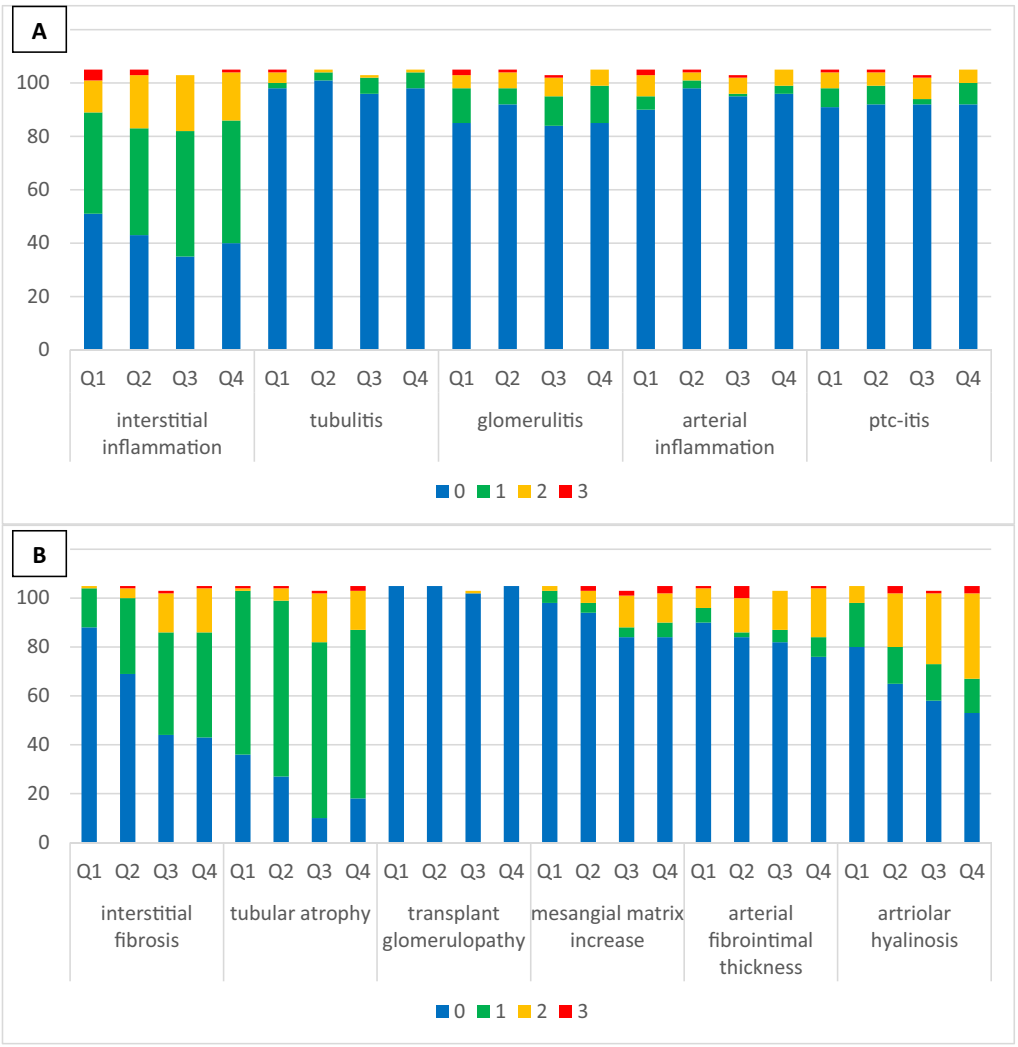


Figure 1: The frequency of the occurrence of specific inflammatory (**A**) or chronic pathologies (**B**).

quartiles ($\chi^2 = 20.8$; $P < .001$). Among the specific pathologies, a similar trend was seen in the percentage of interstitial fibrosis ($\chi^2 = 46.3$; $P < .001$), tubular atrophy ($\chi^2 = 12.9$; $P < .001$), mesangial matrix increase ($\chi^2 = 10.6$; $P < .01$) and arteriolar hyalinosis ($\chi^2 = 15.2$; $P < .001$) (Fig. 1B).

A significant, positive correlation ($R = 0.299$; $P < .001$) between recipient's age and KDRI value was found (Fig. 2A). There was no significant correlation between KDRI value and the semi-quantitatively assessed inflammatory features in the kidney graft biopsy ($R = 0.05$; $P = .29$) (Fig. 2B). In contrast, there was a significant, positive correlation between KRDI value and the semi-quantitatively assessed chronic kidney graft injury ($R = 0.412$; $P < .001$) (Fig. 2C) and the percentage of sclerosed glomeruli ($R = 0.423$; $P < .001$).

The results of univariate analyses are shown in Table 4. Recipient age, retransplantation, the use of induction therapy and KDRI value were significantly associated with chronic biopsy lesions, whereas retransplantation, HLA class II mismatch, KDRI value and very early AR episode were significantly associated with the percentage of sclerotic glomeruli.

Stepwise multivariate regression analysis revealed that only higher KDRI value ($r_{partial} = 0.344$, $P < .001$) independently correlated with the severity of chronic graft injury. Similar analysis performed for the percentage of sclerosed glomeruli showed KDRI value ($r_{partial} = 0.266$; $P < .001$) and HLA class II mismatch ($r_{partial} = 0.104$; $P < .05$) as independent explanatory variables. Other variables were excluded from regression models.

DISCUSSION

In our study, we showed that more advanced chronic histological changes as well as a higher percentage of sclerotic glomeruli were observed in the biopsies of the highest KDRI kidney recipients. Moreover, only a higher KDRI value independently correlated with the severity of chronic graft damage and the percentage of sclerotic glomeruli. These results suggest that the KDRI value in our cohort is an additional predictor of donor kidney baseline status.

At our center, we decided to perform post-reperfusion biopsy to assess the quality of the organs. Since 2015, we have performed protocol graft biopsies during the first hospitalization after kidney transplantation, starting on the eighth postoperative day. The timing of the biopsy was also based on the fact that acute rejection episodes occur most frequently in the first

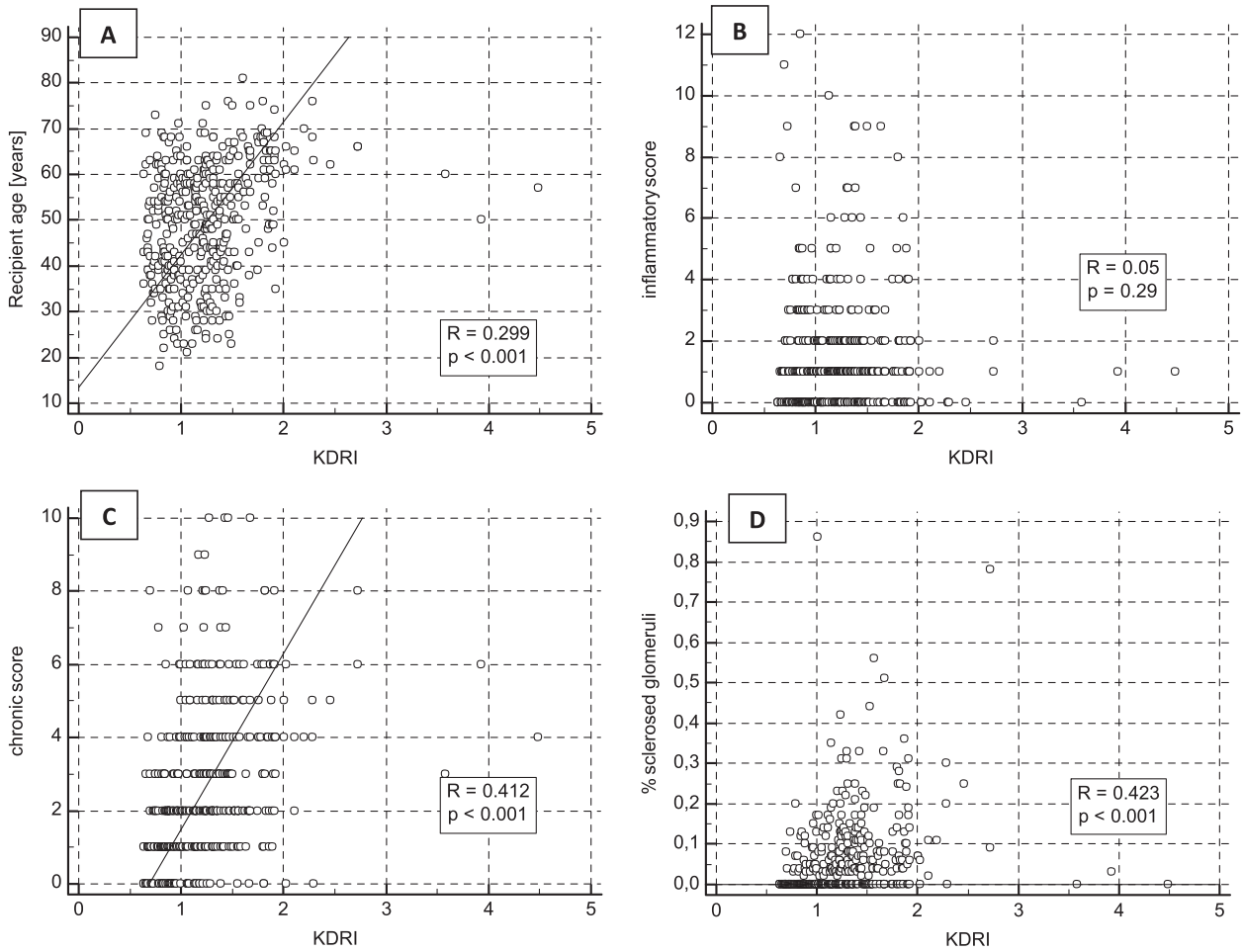


Figure 2: (**A**) Correlation between recipient's age and KDRI value. (**B**) Correlation between KDRI value and the semi-quantitatively assessed inflammatory features in the kidney graft biopsy. (**C**) Correlation between KDRI value and the semi-quantitatively assessed chronic kidney graft injury. (**D**) Correlation between KDRI value and the percentage of sclerotic glomeruli in the kidney graft biopsy.

Table 4: The results of univariate analyses.

	Chronic lesions		Sclerotic glomeruli	
Parameter	β	P	β	P
Recipient age (years)	0.02	<.01	0.0007	.054
BMI (kg/m^2)	0.03	.25	0.0019	.13
Retransplantation	–0.72	<.05	–0.03	<.05
Class II HLA mismatch	0.17	.36	0.03	<.01
Very early AR	–0.42	.21	–0.03	.06
Induction (yes vs no)	0.80	<.01	0.02	.08
KDRI	1.66	<.001	0.06	<.001
Donor age (years)	0.005	.48	–0.0001	.78

Very early AR—episodes of AR diagnosed in the protocol biopsy.

weeks after transplantation, and that serum creatinine concentration may not be the most sensitive marker in early subclinical rejection, as well as taking into account the fact that all biopsy procedures require hospitalization.

In some countries the decision for kidney transplantation from a donor with high KDRI is also based on kidney biopsy findings. It was shown that the use of biopsies in the allocation decision-making process is responsible for 38.2% of kidney discards in the USA [24]. Unfortunately, some studies have revealed that information obtained from procurement biopsies are of low quality [25–28]. They are analyzed using frozen sections obtained by a wedge biopsy technique, which oversamples scarred subcapsular cortex, where more extensive glomerulosclerosis and tubulointerstitial scarring are observed, use a single (hematoxylin and eosin) stain and are interpreted under time-pressure by a pathologist without experience in renal pathology. Reese *et al.* [29] matched 45% of kidneys discarded for abnormal histology in the USA with kidneys with very similar pathologic findings transplanted in France and found that 70% of these matched kidneys were functional after 10 years. This allows the conclusion that the information obtained from the pre-implantation biopsy did not provide substantial value and may lead to unnecessary discard of the kidneys for transplantation. A study by Hall *et al.* [16] has revealed that the Leuven score (calculated from donor age and information from pre-implantation biopsies like precentage of glomerulosclerosis and interstitial/tubular fibrosis) is no better than KDRI for predicting post-transplant survival and graft function. In addition, pre-implantation biopsies may delay decisions and prolong cold ischemia time, which could further injure an already marginal kidney and encourage unnecessary discard.

Another strategy for obtaining renal tissue for histological evaluation of organ quality is to perform a biopsy shortly after reperfusion. Post-reperfusion biopsies, unlike pre-implantation biopsies, are taken with a biopsy needle and then embedded in paraffin, stained following a standard procedure and assessed by a renal pathologist, which is believed to be more accurate in determining the significance of donor histological findings on graft outcomes [18, 19]. Mohan *et al*. [18] have shown in a study of 548 post-reperfusion biopsies by that a suboptimal biopsy was associated with increased probability of delayed graft function and poorer long-term allograft outcomes compared with kidneys with optimal histology, and that the suboptimal histology was more frequently seen in kidneys with higher KDRI values. Carpenter *et al*. [28] showed that procurement biopsies not only are poorly reproducible, but also do not correlate well with reperfusion biopsy findings. Only 64% of procurement and reperfusion biopsies performed in 270 kidneys were classified into the same category (optimal versus suboptimal). It was also shown that post-reperfusion biopsy findings correlate with graft outcomes, but pre-implantation biopsies findings do not [29]. In a systematic review of 47 retrospective studies concerning pre-implantation biopsies, Wang *et al*. [30] showed that no semi-quantitative scoring system was conclusively associated with post-transplant outcomes including DGF, graft function or graft failure.

In this retrospective, single-center analysis we showed that in a Polish transplant cohort higher KDRI values are associated with a higher risk of DGF or SGF in the early post-transplantation period and also with a lower eGFR in follow-up for up to 5 years. Even so, the eGFR in recipients who received the kidneys with the highest KDRI value was at a stable level of 44–47 mL/min/1.73 m^2 over the course of the observation, which is a satisfactory result.

Despite some concerns about the transplant results from ECD, there is an increasing number of kidney transplants from this donor pool. In our study the kidneys with the highest KDRI values were transplanted to older recipients as a consequence of an "old-to-old" allocation program. A recent study showed that in patients older than 60 years as well as in those older than 50 years, kidney transplantation with KDPI >85% was associated with better long-term survival compared with those remaining on the waitlist and potentially receiving a kidney with KDPI 0%–85% [31]. Therefore, transplant using the marginal kidney can be considered a life-saving intervention for appropriate candidates. In a recent study, Park *et al*. [32] examined the impact of KDRI on post-transplant clinical outcomes between elderly and young recipients, and revealed that the high KDRI-young recipients group has worse allograft outcome than the three other groups (i.e. low KDRI-young recipients, low KDRI-elderly recipients and high KDRI-elderly recipients). The impact of high KDRI value on allograft survival may be less significant in the elderly recipients probably due to lower metabolic demand and shorter life-span.

In our study, we showed a positive correlation between the recipient's age and the KDRI value; moreover, recipients who received the highest KDRI kidneys had a higher BMI value, a higher rate of previous MACE and developed PTDM more often during follow-up. All these factors make recipients in the highest KDRI quartile the patients with the highest burden of comorbidity affecting the highest cardiovascular risk. In those recipients of the highest KDRI kidneys, a stable, satisfactory level of eGFR 44–47 mL/min/1.73 m^2 was observed during the follow-up period. In the early post-transplant period, a higher KDRI was associated with a higher risk of DGF or SGF, with the highest incidence (36% and 57%, respectively) in the KDRI Q4 group. We also documented that a lower KDRI value was associated with higher eGFR values throughout the entire follow-up period (the difference in eGFR between KDRI Q1 and Q4 was up to 30 mL/min/1.73 m^2) and IGF occurs in >50% of recipients with the group with the lowest KDRI value (54% vs 12% in recipients from the group with the highest KDRI value). Moreover, there was an increasing trend for the occurrence of combined endpoint (death or graft loss) across KDRI quartiles. We believe that in our cohort, the KDRI value may be a useful additional element in predicting graft function, and our results should encourage the use of KDRI calculations in making allocation decisions.

Limitations of this study include its retrospective, observational design and use of single site registry data. Another limitation is the number of actually performed biopsies compared with the number of patients who were offered a biopsy (418 vs 701). This may be partly due to the fact that in 2015 this biopsy protocol was new and some patients were concerned about having an invasive procedure, especially when creatinine levels were within the normal range. In this study, we were able to assess the eGFR between patients' quartiles and its change over the course of study, however the follow-up was relatively short to examine graft and patient survival after transplantation between KDRI quartiles. As post-transplant graft outcomes such as graft loss and eGFR can be influenced by various factors other than KDRI, not adjusting for confounding factors is a limitation to this study.

In conclusion, KDRI value correlated with chronic histological findings assessed in early post-transplant kidney graft biopsies and can be helpful in predicting graft outcome. It is worth noting that in our study 88% of biopsies had chronic histological changes, the degree of which correlated with the KDRI value. Additionally, this study provides evidence that even a kidney transplant with a high KDRI may result in a reasonably good transplant outcome. We believe that based on our results KDRI may be a useful tool in the Polish population and similar cohorts to assess the quality of deceased donor kidneys, and may be a guide in the allocation decision-making process.

CONFLICT OF INTEREST STATEMENT

None declared.

DATA AVAILABILITY STATEMENT

The data underlying this article will be shared on reasonable request to the corresponding author.

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