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Original Article

ORIGINAL ARTICLE

Tubulo-interstitial inflammation increases the risk of graft loss after the recurrence of IgA nephropathy

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ABSTRACT

Background. Immunoglobulin A nephropathy (IgAN) is the most frequent recurrent disease in kidney transplant recipients and its recurrence contributes to reducing graft survival. Several variables at the time of recurrence have been associated with a higher risk of graft loss. The presence of clinical or subclinical inflammation has been associated with a higher risk of kidney graft loss, but it is not precisely known how it influences the outcome of patients with recurrent IgAN.

Methods. We performed a multicentre retrospective study including kidney transplant recipients with biopsy-proven recurrence of IgAN in which Banff and Oxford classification scores were available. 'Tubulo-interstitial inflammation' (TII) was defined when 't' or 'i' were ≥2. The main endpoint was progression to chronic kidney disease (CKD) stage 5 or to death censored-graft loss (CKD5/DCGL).

Results. A total of 119 kidney transplant recipients with IgAN recurrence were included and 23 of them showed TII. Median follow-up was 102.9 months and 39 (32.8%) patients reached CKD5/DCGL. TII related to a higher risk of CKD5/DCGL (3 years 18.0% vs 45.3%, log-rank 7.588, $P = .006$). After multivariate analysis, TII remained related to the risk of CKD5/DCGL (HR 2.344, 95% CI 1.119–4.910, $P = .024$) independently of other histologic and clinical variables.

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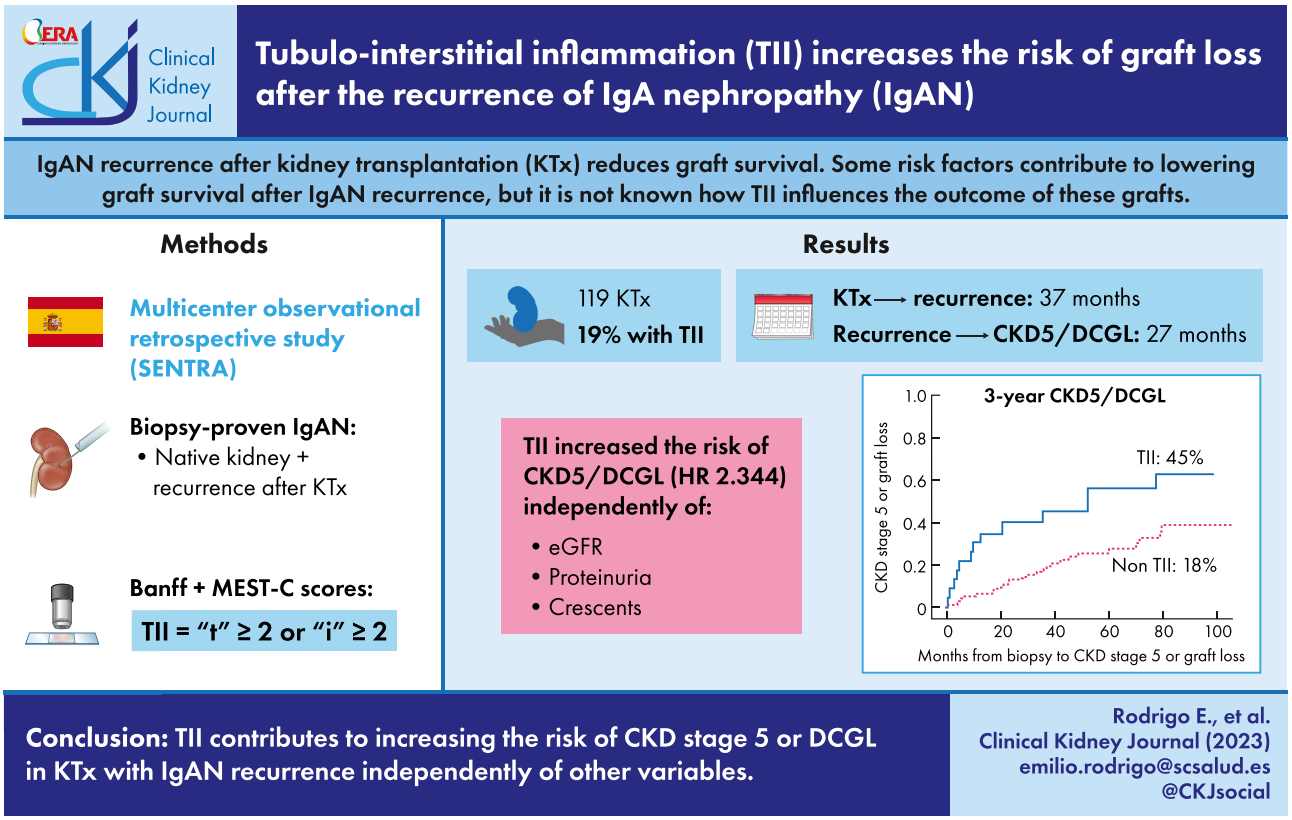
Conclusions. In kidney transplant recipients with IgAN recurrence, TII contributes to increasing the risk of CKD5/DCGL independently of previously well-known variables. We suggest adding TII along with the Oxford classification to the clinical variables to identify recurrent IgAN patients at increased risk of graft loss who might benefit from intensified immunosuppression or specific IgAN therapies.

GRAPHICAL ABSTRACT



Keywords: graft loss, IgA nephropathy, inflammation, kidney transplantation, recurrence

KEY LEARNING POINTS

What was known:

- Immunoglobulin A nephropathy (IgAN) is the most common recurrent disease in kidney transplant recipients and its recurrence reduces graft survival.
- To improve the outcome of kidney transplant recipients, it would be of the utmost interest to identify those kidney transplant recipients at higher risk of suffering a worse outcome after IgAN recurrence.
- Although tubulointerstitial inflammation (TII) related to the alloimmune response has been associated with an increased risk of renal graft loss, it is currently unknown how TII influences the outcome of patients with recurrent IgAN.

This study adds:

- We found that TII was associated with a worse outcome in grafts with recurrent IgAN. This association was independent of other variables related to the evolution of IgAN recurrence, such as GFR, proteinuria and some histological findings.

Potential impact:

- In order to know more accurately the outcome of kidney transplants with IgAN recurrence, TII should be included into the set of already recognized risk variables.
- Moreover, TII must be taken into account in the design of the best therapy for kidney transplant recipients with IgAN recurrence.

INTRODUCTION

Among primary glomerular diseases, immunoglobulin A nephropathy (IgAN) is the most frequent cause of end-stage kidney disease (ESKD) in patients admitted to the waiting list and in those who received an organ transplantation [1]. Moreover, in absolute numbers IgAN is the most frequent recurrent disease in kidney transplant recipients [2]. Although, in the past, it was considered that IgAN recurrence did not have a strong impact on the graft outcome, currently it is known that IgAN recurrence contributes to reducing graft survival beyond 5–10 years after kidney transplantation [3–6]. Due to its frequency and long-term influence, it would be interesting to identify those kidney transplant recipients with a higher risk of suffering a worse outcome after IgAN recurrence.

There are some well identified risk factors for predicting the progression of IgAN in native kidneys. In fact, both clinical and histologic factors such as renal function, blood pressure, proteinuria, race, age, use of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, MEST score and immunosuppression use have been incorporated in a prediction tool (the International IgA Nephropathy (IgAN) Prediction Tool) that is able to discriminate those patients at higher risk of a 50% decline in estimated glomerular filtration rate (eGFR) or ESKD, with a C statistic around 0.8 [7]. By contrast, the predictive value of histologic variables on the graft outcome after IgAN recurrence is controversial. Most studies, but not all, have demonstrated that a higher percentage of crescents at IgAN recurrence worsens graft prognosis [3, 4, 6, 8–11]. Recently, some authors such as Agrawal and Park have reported that the other parameters included in the Oxford classification can be also useful to establish the risk of bad outcome not only in native kidney but also in kidney transplant recipients [10, 12]. However, this finding has not been demonstrated by other authors [6, 11, 13]. Similarly, it is not known if tubulo-interstitial inflammation (TII) has a role on graft evolution after IgAN recurrence. Previous episodes of acute rejection have been related to a lower graft survival after IgAN recurrence [3, 4, 6, 14, 15], but the degree of inflammation at recurrence diagnosis has not been extensively studied [4, 6, 10, 12]. Some authors have highlighted the role of interstitial inflammation in IgAN in the native kidney, although this variable has not been included in the Oxford score [16]. In addition, the presence of both clinical and subclinical alloimmune inflammation in the grafts contributes to deteriorating graft outcome [17–21]. Our hypothesis was that the presence of TII in the graft with IgAN recurrence may increase the risk of graft loss.

MATERIALS AND METHODS

We performed a multicentre observational retrospective study including all renal transplant recipients with biopsy-proven IgAN recurrence in which the Banff and MEST-C scores were available or could be reviewed. All included patients also had biopsy-proven IgAN in their native kidney. Clinical information was retrospectively obtained from the medical history of the patients up to January 2023. IgAN recurrence was defined by the finding of dominant or codominant mesangial deposits of IgA in biopsies for clinical indication. The study was conducted according to the guidelines as dictated by the Declaration of Helsinki and was approved by the ethics committee of University Hospital Marqués de Valdecilla (2019.135).

Transplant collected data were recipient age and gender, donor age and gender, living donation, cold ischaemia time, retransplantation, A, B and DR HLA matching, induction type, delayed graft function and acute rejection during the first year. Delayed graft function was defined as the need for dialysis during the first week following transplantation. Collected data at biopsy were renin–angiotensin–aldosterone system (RAAS) blockade, eGFR, dipstick Hb positivity, 24-h proteinuria, systolic blood pressure, steroid use and dose, and immunosuppressive therapy. Death-censored graft loss (DCGL) was defined as return to dialysis therapy or retransplantation. Chronic kidney disease stage 5 (CKD5) was defined as GFR <15 mL/min/m^2 estimated by the Chronic Kidney Disease Epidemiology Collaboration equation. The main endpoint was progression to CKD stage 5 or to DCGL.

Biopsies were included if had been processed for light microscopy and immunofluorescence and had an adequate sample. The center pathologists examined the graft biopsies using the Banff 2017 classification and the Oxford Classification of IgA nephropathy updated at 2016 [22, 23]. Concurrent T-cell-mediated rejection (TCMR) and antibody-mediated rejection (AbMR) were defined according to the Banff 2017 classification system and revised when needed by the centre's pathologist. TII was defined when Banff scores were 't' ≥ 2 or 'i' ≥ 2.

Continuous variables were expressed as the mean $\pm$ standard deviation. Categorical variables were described as relative frequencies. Kaplan–Meier survival analysis were used to analyse whether TII, TCMR and AbMR related to a higher risk of CKD5 or DCGL. Univariate and multivariate Cox regression models were used to assess the association between variables and the main endpoint. Hazards ratios (HR) were reported with 95% confidence intervals (95% CI). A P-value of $<5\%$ was reported as statistically significant. Statistical analyses were performed with SPSS, version 15.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

One hundred and nineteen kidney transplant recipients with IgAN recurrence demonstrated by kidney graft biopsy between 1996 and 2022 were included. The main characteristics are shown in Table 1. Transplant median follow-up was 102.9 [interquartile range (IQR) 66.4, 152.9] months and median follow-up from transplant to recurrence was 36.8 (IQR 19.9, 92.4) months. Throughout the follow-up, 9 patients (8.5%) died with a functioning graft and 39 (32.8%) patients reached CKD5/DCGL. Median time to graft loss after recurrence was 27.4 (IQR 9.0, 67.2) months.

Twenty-three of the patients (19.3%) showed TII. According to Kaplan–Meier survival analysis, TII related to a higher risk of CKD5/DCGL (3 years 18.0% vs 45.3%, $P = .006$) (Fig. 1). Eight and 12 patients showed concurrent TCMR and histologic AbMR, respectively. All TCMR received steroid or polyclonal antilymphocyte antibodies, whereas six patients with concomitant AbMR received therapy with plasmapheresis (three), rituximab (three) or IVIg (three), or by optimizing immunosuppression restarting prednisone (one) or switching from cyclosporine to tacrolimus (one). Neither TCMR (HR 1.131, 95% CI 0.346–3.698, $P = .838$) nor AbMR (HR 1.995, 95% CI 0.770–5.166, $P = .155$) was associated with a higher risk of CKD5/DCGL.

Patients with TII had suffered more frequently acute rejection throughout the first year (27.3% vs 6.3%, $P = .003$) and were treated with mycophenolic acid or mycophenolate mofetil less frequently (73.9% vs 90.6%, $P = .030$).

Univariate and multivariate Cox regression analysis of variables at recurrence related to CKD5/DCGL are shown in Table 2. Non-use of tacrolimus, systolic blood pressure, eGFR, the logarithm of proteinuria at recurrence, TII, C4d deposition in peritubular capillaries, 'ptc' Banff score and 'T' and 'C' and

Table 1: Main baseline characteristics of kidney transplant recipients with IgAN recurrence.

Number of IgAN recurrent patients	119
Recipient age at recurrence (years) (mean ± SD)	46.6 ± 13.8
Recipient sex (male) (%)	79.0
Donor age (years) (mean ± SD)	44.5 ± 15.6
Donor sex (male) (%)	72.3
Living donation (%)	16.8
Cold ischemia time (h) (mean ± SD)	14.1 ± 7.5
Retransplant (%)	15.1
Mismatches A-B-DR (mean ± SD)	3.6 ± 1.2
Thymoglobulin induction (%)	39.5
Basiliximab induction (%)	28.6
Delayed graft function (%)	23.5
First year acute rejection (%)	10.1
RAAS blockade at biopsy (%)	72.3
Estimated GFR at biopsy (mL/min/1.73 m^2) (mean ± SD)	45.4 ± 17.9
Dipstick Hb positivity (%)	88.2
24-h proteinuria (gram/day) (mean ± SD)	1.6 ± 1.7
Proteinuria >1 g/day at biopsy (%)	59.7
Systolic blood pressure (mmHg) (mean ± SD)	137 ± 15
Steroid use at biopsy (%)	82.4
Daily prednisone dose at biopsy (mg) (mean ± SD)	5.3 ± 6.1
Tacrolimus use at biopsy (%)	86.6
Cyclosporine use at biopsy (%)	9.2
Azathioprine use at biopsy (%)	3.4
Mycophenolate/mycophenolic use at biopsy (%)	87.4
mTOR inhibitor at biopsy (%)	10.1
g 0/1/2/3 (%)	53.8/29.4/15.1/1.7
i 0/1/2/3 (%)	45.4/41.2/13.4/0.0
t 0/1/2/3 (%)	57.1/32.8/9.2/0.8
t ≥ 2 or i ≥ 2 (%)	19.3
v 0/1/2/3 (%)	94.1/5.0/0.8/0.0
ptc 0/1/2/3 (%)	77.3/16.0/6.7/0.0
ci 0/1/2/3 (%)	21.0/52.1/23.5/3.4
ct 0/1/2/3 (%)	22.7/51.3/22.7/3.4
ptc C4d peposition positivity (%)	13.4
M 0/1 (%)	30.3/69.7
E 0/1 (%)	63.9/36.1
S 0/1 (%)	44.5/55.5
T 0/1/2 (%)	37.8/57.1/5.0
C 0/1/2 (%)	77.3/19.3/3.4
MEST-C (mean ± SD)	2.6 ± 1.5

SD, standard deviation.

'MEST-C' were related to a higher risk of CKD5/DCGL. In a multivariate model including only statistically significant histologic variables, TII and 'C' remained independently related to a higher risk of CKD5/DCGL (Table 2). A second model including clinical variables found that both eGFR and the logarithm of proteinuria were independently associated with CKD5/DCGL. Last, in a third model including both histologic independent variables such as TII and 'C' and clinical variables such as eGFR and the logarithm of proteinuria, TII remained independently related to the risk of CKD5/DCGL (Table 2). Excluding eight patients who showed histological criteria of TCMR at the recurrence diagnosis, TII remained independently related to a higher risk of CKD5/DCGL (HR 3.433, 95% CI 1.530–7.704, $P = .003$) independently of other variables.

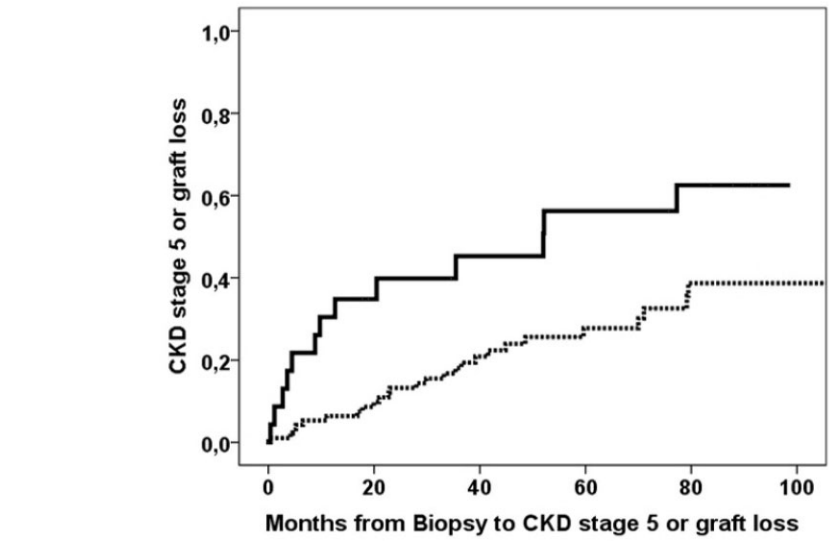
After recurrence, immunosuppression was increased in 50 patients (42.3%): high-dose steroid (prednisone >20 mg/day) was used in 43 patients (36.1%) and baseline immunosuppression was optimized (restarting prednisone, switching to mycophenolate or tacrolimus) in 13 (10.9%) patients. Two patients were treated with cyclophosphamide together with the steroid therapy. This immunosuppression enhancement was related to a worse graft survival in univariate analysis but did not have a significant effect after adjusting by GFR, or histologic variables. RAAS blockade was added or increased in 32 (26.9%) patients.

DISCUSSION

Primary glomerular disease recurrence after kidney transplantation has a strong impact on the graft outcome [2]. Regarding transplant recipients with ESKD due to IgAN, its recurrence is the third cause of graft loss after death with a functioning graft and chronic rejection [24]. In our study, a third of the patients suffered graft loss after a median time of 27 months. Previous studies have reported a median time from IgAN recurrence to graft loss between 25 and 106 months [4, 5, 24–26]. Being the most frequent cause of glomerular disease recurrence after kidney transplantation and contributing to graft loss, it is of the utmost interest to determine the risk factors for a bad outcome to identify which patients could benefit most from any specific therapies. In fact, new promising treatments for IgAN are being developed that could improve its outcome and some of them are already beginning to be used in kidney transplant recipients with IgAN recurrence [27, 28].

Among other well-recognized risk factors, we identified that interstitial inflammation and/or tubulitis were related to a higher risk of CKD5 or DCGL. This relationship was found both in univariate and multivariate analysis independently of some clinical strong predictors of bad outcome such as eGFR, proteinuria and blood pressure, and histologic variables included in the Oxford classification for IgAN. In fact, TII increased the risk of graft loss by more than two times. This finding has not been previously reported, although Agrawal *et al*. described that interstitial inflammation was associated with a worse transplant outcome in univariate analysis performed in a study including 22 kidney transplant recipients with recurrent IgAN [12]. Some studies have analysed the influence of rejection concurrent with IgAN recurrence after kidney transplantation. Kavanagh *et al*. found that acute rejection including both TCMR and AbMR was present in 20% of biopsies concurrently with IgAN recurrence and was independently associated with a higher risk of allograft failure (HR 3.51, 95% CI 1.11–11.0, $P = 0.03$) [6]. By contrast, Park *et al*. reported that coexisting acute rejection was not independently related to a higher risk of graft loss after IgAN recurrence [4, 10]. Although we detected that 'ptc' and C4d deposition were associated with a higher risk of the study endpoint in univariate analysis, both variables did not remain significant after multivariate analysis in this group of kidney transplant recipients with IgAN recurrence. Differently from these studies, we analysed all the individual Banff scores for the first time in a large number of recurrent patients. The fact that more severe cellular inflammation enough to be classified as TCMR according to the Banff scheme was not associated with a higher risk of the endpoint in our study must be due to that those patients received specific therapy for treating the TCMR.

There is supporting evidence that low-grade graft inflammation not qualifying as rejection according to Banff criteria worsens the long-term prognosis of kidney transplantation. Both borderline and subclinical inflammation has been associated with *de novo* DSA development, fibrosis progression and an increased risk of long-term graft loss [17–20]. Moreover, Mehta *et al*. have reported that even borderline subclinical changes were



Number at risk						
No Inflammation	96	79	53	34	19	9
Inflammation	23	13	10	8	6	0

Figure 1: CKD5/graft loss development according to the presence (continuous line) or not (dashed line) of tubulointerstitial inflammation (log-rank 7.588, $P = .006$).

associated with a greater hazard for subsequent clinical acute rejection and long-term censored graft loss [21]. Our study found that TII contributes to worsening graft outcome in kidney transplant recipients with recurrent glomerular disease. This inflammation is predictably related to the alloimmune response against the graft that could be occurring simultaneously to the autoimmune response that causes the recurrence. The fact that patients with previous acute rejection episodes showed TII at IgAN recurrence more frequently supports the idea that incompletely solved alloimmune response can perpetuate in time, promoting fibrosis and leading to long-term graft loss [17, 29]. Less likely, the inflammation that we found may be due to autoimmunity itself. The fact that a higher level of interstitial inflammation is associated with a higher rate of kidney function decline in patients with IgAN in the native kidney has been described by Zhu *et al*., being a frequent finding in other primary glomerular diseases [16]. Immunosuppressive therapy probably reduces the degree of TII, but, just as it does not stop the appearance of glomerular damage, it cannot be ruled out that a certain degree of concurrent inflammation appears together with glomerular damage.

Finally, klotho deficiency has been associated with increasing release of proinflammatory cytokines such as TNF (tumour necrosis factor) and TWEAK (TNF-like weak inducer of apoptosis) [30], which can increase in the presence of allograft inflammation. Thus, we cannot rule out that a lower klotho expression due to immunological graft dysfunction might be the cause of higher fibrosis and tubular atrophy. We choose a cut-off of $i \geq 2$ or $t \geq 2$ for defining intragraft TII in order to exclude a lower degree of inflammation such as isolated interstitial inflammation (i1) or tubulitis (t1). This well might be associated with lower variability among pathologists. In any case, with our study design, it would not be possible to know the underlying cause of the detected TII.

Together with TII, we found that renal function, proteinuria and blood pressure were independently related to a higher risk of CKD5 or DCGL. These variables are well-recognized risk factors for the poor outcome not only in glomerular nephropathies in the native kidney but also in renal transplantation with and without recurrence of primary glomerular disease [2, 4, 6, 7]. Interestingly, we found that some variables included in the Oxford classification for IgAN were also related to the graft outcome. In univariate analysis, both 'T' and 'C' were associated with graft evolution, whereas in the multivariate analysis, only the percentage of crescents did have an influence on the risk of CKD5 or DCGL. By contrast, 'M', 'E' and 'S' had no impact. The use of immunosuppression could be influencing the fact that these three items were not related to the evolution of the graft, although the study carried out by Park *et al*. reported that 'M', 'E' and 'S', but not 'T' influenced on a worse outcome together with the percentage of crescents score according to the Oxford classification independently of renal function, albuminuria, TCMR and AbMR [4, 10]. It cannot be ruled out that the sample size influenced these results because some smaller studies have detected variable relationships between each item of the classification and the evolution after recurrence [5, 6, 12]. For instance, Kavanagh *et al*. reported that only 'T' and 'S' related to the risk of graft loss after IgAN recurrence, but only in the univariate analysis [6], while Agrawal *et al*. found that only 'E' and 'T' scores were associated with graft outcome [12] and Uffing *et al*. did not find a relationship between mesangial proliferation and graft survival after recurrence [5]. On the other hand, the influence of 'E' is discussed even in native kidney, having been identified the fact that the use of immunosuppression may mask the predictive value of 'E' in renal outcomes [23].

Of interest, increasing 'C' scores doubled the risk of CKD5 or DCGL independently of other variables. Hence, the percentage of crescents seems more determinant in the kidney graft than in the native kidney [4, 8, 9, 11, 31]. It would be tempting to think that commonly used immunosuppression does not at all slow the development of crescents once IgAN recurs. We suggest adding Oxford classification or at least the crescent percentage

Table 2: Univariate and multivariate Cox regression analysis of variables related to CKD5/DCGL.

	Univariate Cox regression analysis (HR, 95% CI)	Model 1 multivariate Cox regression analysis (HR, 95% CI)	Model 2 multivariate Cox regression analysis (HR, 95% CI)	Model 3 multivariate Cox regression analysis (HR, 95% CI)
Recipient age at recurrence (years)	0.998, 0.976–1.021, $P = .879$			
Recipient sex (male)	1.613, 0.676–3.851, $P = .281$			
Donor age ≥55 years	0.895, 0.451–1.776, $P = .750$			
Living donation	0.959, 0.401–2.292, $P = .925$			
Cold ischaemia time (h)	1.017, 0.972–1.065, $P = .463$			
Retransplant	1.455, 0.690–3.068, $P = .324$			
Mismatches A-B-DR	1.166, 0.888–1.532, $P = .270$			
Thymoglobulin induction	0.607, 0.302–1.220, $P = .161$			
Basiliximab induction	1.307, 0.694–2.573, $P = .385$			
Delayed graft function	1.706, 0.876–3.320, $P = .116$			
First year acute rejection	1.748, 0.731–4.184, $P = .209$			
RAAS blockade at biopsy	0.866, 0.451–1.663, $P = .666$			
eGFR at biopsy (mL/min/1.73 m^2)	0.951, 0.927–0.976, $P < .001$		0.946, 0.919–0.973, $P < .001$	0.955, 0.928–0.982, $P = .002$
Logarithm of 24-h proteinuria (g/day)	11.015, 4.088–29.678, $P < .001$		10.630, 3.947–28.627, $P < .001$	7.345, 2.282–23.646, $P = .001$
Systolic blood pressure (mmHg)	1.040, 1.017–1.064, $P = .001$			
Steroid use at biopsy	0.640, 0.311–1.316, $P = .225$			
Daily prednisone dose at biopsy (mg)	0.962, 0.882–1.050, $P = .384$			
Tacrolimus use at biopsy	0.438, 0.201–0.957, $P = .038$		0.970, 0.415–2.269, $P = .945$	
Cyclosporine use at biopsy	2.275, 0.887–5.836, $P = .087$			
Azathioprine use at biopsy	3.411, 0.813–14.310, $P = .094$			
Mycophenolate/mycophenolic use at biopsy	0.595, 0.248–1.423, $P = .243$			
mTOR inhibitor at biopsy	1.016, 0.360–2.866, $P = .975$			
t ≥ 2 or i ≥ 2	2.480, 1.271–4.838, $P = .008$	2.644, 1.204–5.806, $P = .015$		2.344, 1.119–4.910, $P = .024$
v	1.038, 0.388–2.778, $P = .941$			
ptc	1.634, 1.031–2.589, $P = .037$	1.536, 0.926–2.549, $P = .096$		
C4d deposition positivity	2.506, 1.142–5.502, $P = .022$			
M	1.053, 0.523–2.120, $P = .886$			
E	1.290, 0.685–2.430, $P = .430$			
S	1.055, 0.559–1.991, $P = .869$			
T	2.166, 1.158–4.051, $P = .016$	1.232, 0.649–2.338, $P = .523$		
C	3.300, 2.012–5.412, $P < .001$	3.788, 2.228–6.438, $P < .001$		4.376, 1.160–16.510, $P = .029$
MESTC	1.357, 1.080–1.704, $P = .009$			

Model 1: only histologic significant variables.
Model 2: only clinical variables.
Model 2: histologic and analytical significant variables.

and TII to perform a more accurate prediction of the risk of graft loss of IgAN recurrent recipients.

The main limitations of this study are related to the fact that it is a multicentre retrospective observational study. Patients were included over a long period of time in that not only immunosuppressive therapy, but also general healthcare evolved strikingly. Evaluation of some information such as anti-HLA antibodies at the recurrence changed throughout the study and was not recorded in the former patients. Because pre-transplant or procurement biopsies were not performed systematically and prospectively in most centres and patients, we have not been able to adequately assess whether some glomerular abnormalities or other histological abnormalities were pre-existing in the donor. The differences in the criteria for indicating graft biopsies between centres, in the anatomopathological evaluation and in the treatments performed could cause biases in the interpretation of the results. On the other hand, these differences are related to the real-life practice. With our study, a causal relationship between TII and poor graft evolution cannot be inferred without carrying out subsequent prospective studies. Of interest, the International IgA Nephropathy Network is embarking on a global study to address these questions using the same methodology as for the Oxford classification. Besides, a survey has already been sent out to nephrologists and pathologists asking about clinical/pathology practice around recurrent IgAN.

Among the strengths of our study, we included a significant number of patients with IgA demonstrated in renal biopsy both in the graft and in the native kidney, with a comprehensive evaluation of histological lesions by both the Banff and Oxford classifications and without losses of follow-up.

To conclude, in a kidney transplant recipient population with IgAN recurrence demonstrated by graft biopsy, we found that TII contributes to increasing the risk of CKD5 or DCGL independently of previously well-known variables such as renal function, proteinuria, blood pressure and the percentage of crescents. Based on our study, we would suggest that, in order to stratify the risk of worsening of kidney transplant recipients with IgAN recurrence and establish in which patients it might be more useful to start a specific treatment for recurrence, we should incorporate not only the usual clinical markers, but also TII together with the Oxford classification and, within it, specifically the percentage of crescents.

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DATA AVAILABILITY STATEMENT

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

CONFLICT OF INTEREST STATEMENT

None declared.

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