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Association of Circulating 25-Hydroxyvitamin D and Recurrence of Glomerulonephritis in Kidney Transplant Recipients: The Wisconsin Allograft Recipient Database (WisARD)

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Background. Recurrence of glomerulonephritis (GN) is a significant contributor to long-term allograft failure among kidney transplant recipients (KTRs) with kidney failure because of GN. Accumulating evidence has revealed the role of vitamin D in both innate and adaptive immunity. Although vitamin D deficiency is common among KTRs, the association between 25-hydroxyvitamin D (25[OH]D) and GN recurrence in KTRs remains unclear. **Methods.** We analyzed data from KTRs with kidney failure caused by GN who received a transplant at our center from 2000 to 2019 and had at least 1 valid posttransplant serum 25(OH)D measurement. Survival analyses were performed using a competing risk regression model considering other causes of allograft failure, including death, as competing risk events. **Results.** A total of 67 cases of GN recurrence were identified in 947 recipients with GN followed for a median of 7.0 y after transplant. Each 1 ng/mL lower serum 25(OH)D was associated with a 4% higher hazard of recurrence (subdistribution hazard ratio [HR]: 1.04; 95% confidence interval [CI], 1.01-1.06). Vitamin D deficiency (≤20 ng/mL) was associated with a 2.99-fold (subdistribution HR: 2.99; 95% CI, 1.56-5.73) higher hazard of recurrence compared with vitamin D sufficiency (≥30 ng/mL). Results were similar after further adjusting for concurrent urine protein–creatinine ratio, serum albumin, and estimated glomerular filtration rate (eGFR). **Conclusions.** Posttransplant vitamin D deficiency is associated with a higher hazard of GN recurrence in KTRs. Further prospective observational studies and clinical trials are needed to determine any causal role of vitamin D in the recurrence of GN after kidney transplantation. More in vitro and in vivo experiments would be helpful to understand its effects on autoimmune and inflammation processes.

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Short-term allograft survival has improved significantly with better immunosuppression agents in the past few decades.[1] Recurrence of glomerulonephritis (GN) is a rising concern with the extension of allograft survival.[2-4] Disease recurrence is the third leading cause of 10-y allograft failure among kidney transplant recipients (KTRs) with GN as the cause of end-stage kidney disease (ESKD),[5] although the reported incidence of GN recurrence varies substantially across different registries which vary in follow-up time, biopsy policies, and distributions of specific GNs.[2,4,6-10]

Immune processes play a crucial role in the pathogenesis of a wide spectrum of primary GN diseases.[11] Autoimmune GNs characterized by glomerular deposits of autoantibodies either occur in the context of systemic autoimmune diseases (eg, lupus nephritis, antineutrophil cytoplasmic antibody [ANCA]-associated vasculitis), develop as a result of renal deposition of immune complexes (eg, immunoglobulin A nephropathy [IgAN]), or result from autoimmune response targeting self-antigens expressed exclusively in the kidney (eg, anti-glomerular basement membrane [anti-GBM] disease, membranous nephropathy). Emerging evidence indicates that multiple immune cells may be involved in the initiation and progression of primary focal segmental glomerulosclerosis (FSGS), although circulating factors are proposed to be the major cause of podocyte damage.[12]

In addition to the classical roles in calcium homeostasis and bone metabolism, vitamin D also is an immunomodulating hormone.[13,14] Vitamin D receptors and metabolism enzymes are widely expressed by various immune cells.[15-17] Experimental studies have demonstrated multiple immune properties of vitamin D in both innate and adaptive immunity, especially its potential to promote self-tolerance.[18] Over 50% of KTRs are insufficient in vitamin D during the first year after transplant[19-22] and serum 25-hydroxyvitamin D (25[OH]D) remains low even several years after transplant in many KTRs.[23,24]

We investigated the association between posttransplant serum 25(OH)D and the incidence of recurrent GN in a cohort of KTRs with GN as the cause of ESKD.

MATERIALS AND METHODS

Study Population

The Wisconsin Allograft Recipient Database is an ongoing longitudinal cohort collecting information on all solid organ transplants performed at the University of Wisconsin (UW).[25] Adult KTRs (≥18 y old) with biopsy-proven GN as the cause of ESKD who received a kidney-only transplant at UW from January 1, 2000 to December 31, 2019, were eligible for this study. Only the most recent transplant for each recipient within the study period was included to maintain independence among transplants. Recipients without any valid posttransplant serum 25(OH)D measurement during the study period were excluded. Recipients who experienced recurrence or allograft failure before the first eligible serum 25(OH)D measurement also were excluded. This study was approved by the UW Health Sciences Institutional Review Board.

Primary GN and Recurrence

The cause of ESKD was identified via medical history at the time of transplantation. Eligible GN diseases included hemolytic uremic syndrome, FSGS, IgAN, proliferative GN, membranous nephropathy (MN), membranoproliferative glomerulonephritis (MPGN), rapidly progressive GN, minimal change GN, anti-GBM disease, ANCA-associated vasculitis, and lupus nephritis. Recipients were followed from the first posttransplant 25(OH)D measurement until disease recurrence, allograft failure (ie, resumption of dialysis, retransplant, or death), or the date of last available data (August 22, 2022), whichever came first. Recurrence of GN was confirmed by biopsy following abnormal clinical signs or laboratory tests.

Measurements

All posttransplant serum 25(OH)D measurements (the total of $25(OH)D_2$ and $25(OH)D_3$) from the UW Hospital and Clinics Clinical Laboratory and other qualified laboratories were collected, where serum 25(OH)D was measured using liquid chromatography-tandem mass spectrometry. Results of serum 25(OH)D lower than the detectable threshold (ie, 5 ng/mL) were excluded. Vitamin D deficiency and insufficiency were defined as serum 25(OH)D ≤ 20 ng/mL (50 nmol/L), and 21–29 ng/mL (52.5–72.5 nmol/L), respectively, in accordance with the Endocrine Society Clinical Practice Guidelines.[26] Measurement time of 25(OH)D was counted as months after transplantation. Demographics (age at transplant, sex, race), previous kidney transplant, and donor characteristics also were collected. Measurements of urine protein–creatinine ratio (UPCR), serum albumin, and serum creatinine within 1 wk of 25(OH)D measurements were collected when available.

Statistical Analysis

Descriptive analyses were conducted for baseline characteristics at the time of transplantation. Cumulative incidence of recurrence was calculated and depicted via the Kaplan-Meier method. Bivariate and multivariate competing risk regression models based on Fine and Gray's proportional hazards model[27] were applied, including events within 1 y after each serum 25(OH)D measurement. Allograft failure due to death or other causes except for recurrence were regarded as competing risk events. Posttransplant serum 25(OH)D was analyzed as a time-varying covariate. Recipient age at transplant, sex, race, donor status, prior kidney transplant, and measurement time of serum 25(OH)D (ie, months after transplant) were included in multivariate models. The proportional hazards assumption was tested by adding an interaction with time. Robust standard errors were obtained considering correlation among repeated measurements for the same recipient. Adjusted subdistribution hazard ratio (HR) was calculated using the competing risk model, where 25(OH)D level was fitted using natural cubic spline with knots at 5, 35, 65, and 95 percentiles. Subgroup analyses were performed by specific GN diseases. Covariates adjusted in subgroup analysis were limited to those statistically significant in the full model due to relatively limited sample size.

Secondary analyses were further adjusted for concurrent UPCR, serum albumin, and creatinine-based-estimated glomerular filtration rate (eGFR) where available. Sensitivity analyses excluded the first month after each serum 25(OH)D measurement from the period at risk to assess the potential impact of reverse causality. All analyses were performed using Stata Statistical Software Release 17.0 (www.stata.com).

RESULTS

A total of 1109 patients with GN as the cause of ESKD received a kidney transplant at our center from January 1, 2000, to December 31, 2019. Among them, 947 recipients had at least 1 valid posttransplant serum 25(OH)D measurement with a functioning allograft and were included in our study (Figure 1). The most common GN was IgAN (n = 315, 33%), followed by FSGS (n = 270, 29%), lupus nephritis (n = 141, 15%), MN (n = 56, 6%), and MPGN (n = 45, 5%) (Table 1). There was an average of 5 posttransplant 25(OH)D measurements (interquartile range [IQR]: 3–9) for each eligible recipient. Their first 25(OH)D measurement was approximately 6 mo after transplant on average. Roughly 18% and 25% of recipients had vitamin D deficiency (25[OH]D ≤ 20 ng/mL) and insufficiency (21–29 ng/mL), respectively, at the time of the first posttransplant 25(OH)D measurement. The level of circulating vitamin D was lower among recipients who were younger at the time of transplant or non-White. Recipients were followed for a median of 7.0 y after transplant (IQR: 4.1–11.0).

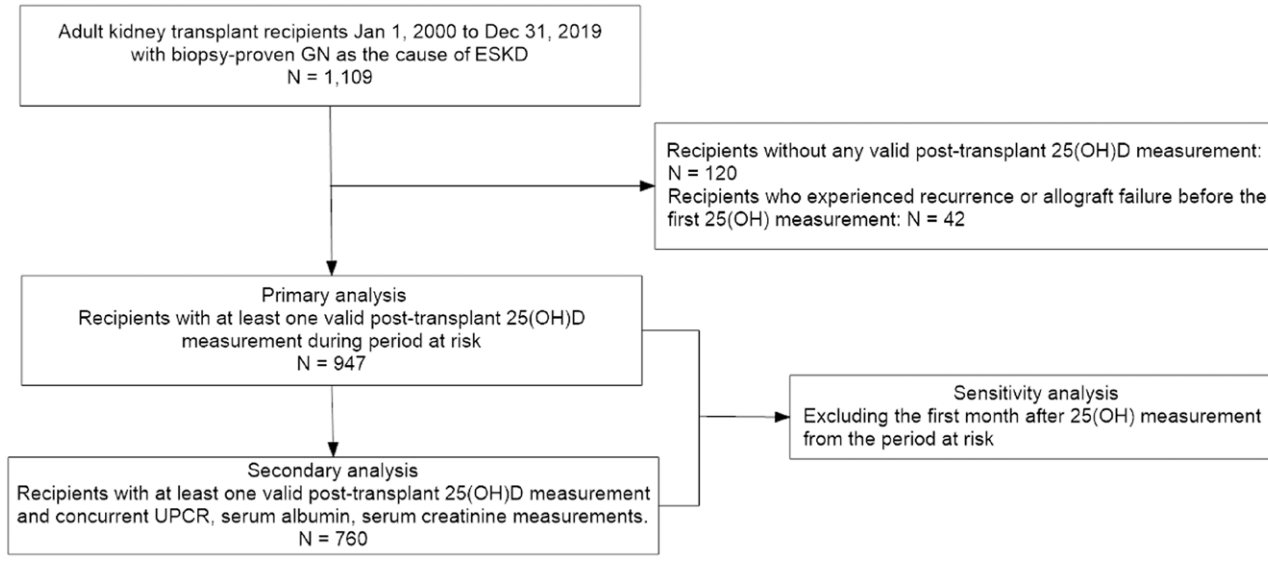

FIGURE 1. Study design. The flowchart outlines the selection of the study population and corresponding analyses. 25(OH)D, 25-hydroxyvitamin D; ESKD, end-stage kidney disease; GN, glomerulonephritis; UPCR, urine protein–creatinine ratio.

TABLE 1.

Characteristics of overall study population

Characteristics	Total	Serum 25(OH)D[a] ≤20 ng/mL	21–29 ng/mL	≥30 ng/mL	*P*
Number of kidney transplant recipients	n = 947	n = 174	n = 240	n = 533	
Age at transplant, yr	47 (13)	44 (12)	47 (13)	48 (13)	0.01
Female, %	431 (46)	92 (53)	114 (48)	225 (42)	0.04
Race, %					0.01
White	727 (78)	120 (69)	191 (80)	426 (80)	
Non-White	210 (22)	54 (31)	49 (20)	107 (20)	
Primary GN, %					0.08
Focal segmental glomerulosclerosis	270 (29)	55 (32)	67 (28)	148 (28)	
IgA nephropathy	315 (33)	50 (29)	87 (36)	178 (33)	
Membranous nephropathy	56 (6)	11 (6)	15 (6)	30 (6)	
Membranoproliferative glomerulonephritis	45 (5)	14 (8)	12 (5)	19 (4)	
Lupus nephritis	141 (15)	30 (17)	35 (15)	76 (14)	
Other GNs[b]	120 (12)	14 (8)	24 (10)	82 (15)	
Living donor, %	390 (41)	60 (35)	104 (43)	226 (42)	0.14
Prior kidney transplant, %	213 (23)	43 (25)	60 (25)	110 (21)	0.30
First 25(OH)D measurement time, months after transplant[c]	6.4 (0.8–15.6)	6.0 (0.6, 30.1)	5.3 (0.7–13.9)	6.5 (1.0–s15.3)	0.10

Continuous variables were presented as mean (SD). Categorical variables were presented as count (percentage).
[a]First serum 25(OH)D measurement after transplant.
[b]Other glomerulonephritis (GNs) included hemolytic uremic syndrome, rapidly progressive GN, anti-glomerular basement membrane disease, and antineutrophil cytoplasmic antibody-associated vasculitis.
[c]The first serum 25(OH)D measurement time after transplant was presented as median (interquartile range).
25(OH)D, 25-hydroxyvitamin D; GN, glomerulonephritis.

Incidence of Recurrent GN

A total of 67 cases of recurrent GN were identified during follow-up, including 20 cases of recurrent FSGS, 26 cases of recurrent IgAN, 9 cases of recurrent MN, 5 cases of recurrent MPGN, and 5 cases of recurrent lupus nephritis. They were diagnosed at a median of 4.6 y after transplant (IQR: 0.9–8.7). The cumulative incidence was estimated to be 12% during 15 y after transplant. The 15-y cumulative incidence of recurrence was estimated to be 10%, 17%, 19%, 15%, and 8% for FSGS, IgAN, MN, MPGN, and lupus nephritis, respectively (Figure 2).

Association of Vitamin D With Recurrent GN

One ng/mL lower serum 25(OH)D level was associated with 4% higher hazard of recurrence (subdistribution HR: 1.04; 95% confidence interval [CI], 1.01-1.06) after adjusting for age at transplant, sex, race, donor status, prior kidney transplant, and measurement time of 25(OH)D (Table 2). Vitamin D deficiency was associated with a 2.99-fold higher hazard of recurrence (subdistribution HR: 2.99; 95% CI, 1.56-5.73) compared with vitamin D sufficiency. The association of lower post-transplant 25(OH)D level with higher hazard of recurrence was relatively linear with no apparent threshold detected (Figure 3).

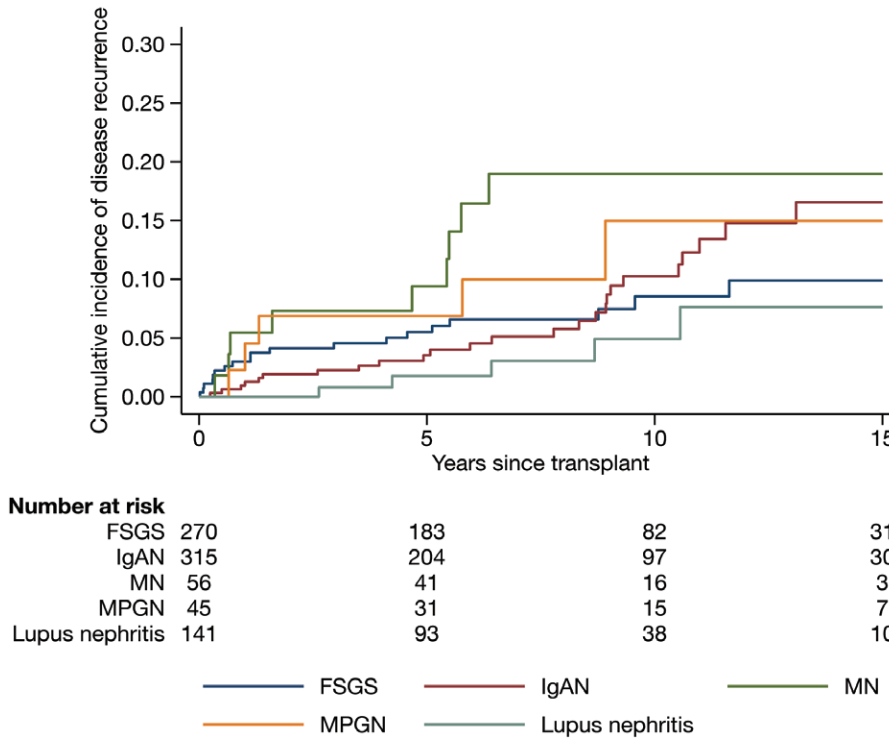

FIGURE 2. Cumulative incidence of recurrence of specific glomerulonephritis (GN) across years after transplant in overall study population. 25(OH)D, 25-hydroxyvitamin D; FSGS, focal segmental glomerulosclerosis; IgAN, IgA nephropathy; MPGN, membranoproliferative glomerulonephritis; MN, membranous nephropathy.

TABLE 2.

Association between posttransplant 25(OH)D and recurrence of glomerulonephritis

Analyses	Sample size	Serum 25(OH)D[a]	Subdistribution HR (95% CI)[b]	
			Unadjusted	Adjusted[c]
Primary analyses[d]	947 KTRs (67 events)	Per ng/mL lower	1.04 (1.01-1.06)	1.04 (1.01-1.06)
		Sufficiency (≥30 ng/mL)	Reference	Reference
		Insufficiency (21–29 ng/mL)	1.50 (0.84-2.67)	1.46 (0.80-2.66)
		Deficiency (≤20 ng/mL)	2.89 (1.59-5.25)	2.99 (1.56-5.73)
Secondary analyses[e]	760 KTRs (48 events)	Per ng/mL lower	1.05 (1.02-1.08)	1.03 (1.00-1.07)
		Sufficiency (≥30 ng/mL)	Reference	Reference
		Insufficiency (21–29 ng/mL)	1.41 (0.71-2.79)	1.11 (0.52-2.34)
		Deficiency (≤20 ng/mL)	3.32 (1.65-6.67)	2.51 (1.13-5.55)

25(OH)D, 25-hydroxyvitamin D; HR, hazard ratio; CI, confidence interval; KTR, kidney transplant recipient.

[a]Posttransplant serum 25(OH)D was analyzed as a time-varying covariate.

[b]Competing risk regression model was fitted with allograft failure due to other causes (including death) as competing events. One year after each serum 25(OH)D measurement was regarded as a period at risk.

[c]Models were adjusted for recipient age at transplant, sex, race, donor status, prior kidney transplant, and measurement time of serum 25(OH)D (ie, months after transplant) in primary analyses; models were further adjusted for concurrent urine protein–creatinine ratio (UPCR), serum albumin, and estimated glomerular filtration rate in secondary analyses.

[d]Primary analyses were conducted in the total study population.

[e]Secondary analyses were conducted in the study population where concurrent measurements of UPCR, serum albumin and serum creatinine were available.

Secondary Analyses

A total of 48 recurrent cases were identified among 760 eligible recipients with concurrent measurements of UPCR, serum albumin, and serum creatinine (Table S1, **SDC**, http://links.lww.com/TXD/A627). It was found that recipients with higher levels of UPCR, lower levels of serum albumin, and lower eGFR have lower levels of circulating 25(OH)D as expected. The association between 25(OH)D and GN recurrence remained significant after further adjusting for concurrent UPCR, serum albumin, and eGFR (Table 2). One ng/mL lower serum 25(OH)D level was associated with 3% higher hazard of recurrence (subdistribution HR: 1.03; 95% CI, 1.00-1.07). Vitamin D deficiency was associated with a 2.51-fold higher hazard of recurrence (subdistribution HR: 2.51; 95% CI, 1.13-5.55) compared with vitamin D sufficiency.

Stratified Analyses

Although the sample sizes were small, there was some evidence of variation in the strength of the association across specific GNs (Table 3). Each 1 ng/mL lower 25(OH)D was associated with an 8% higher hazard of recurrent FSGS (subdistribution HR: 1.08; 95% CI, 1.03-1.12). Vitamin D deficiency was associated with a 5.3-fold higher hazard of

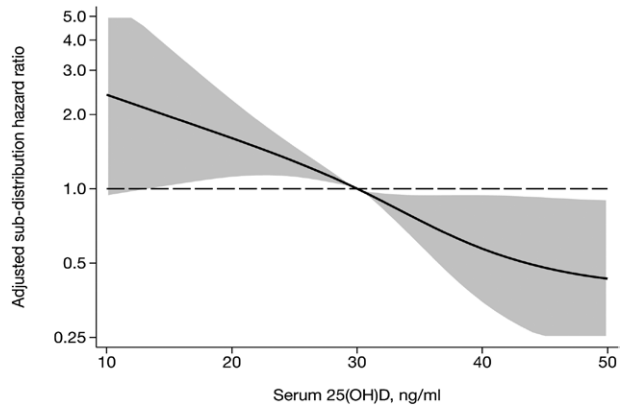

FIGURE 3. Adjusted subdistribution hazard ratio of recurrence of glomerulonephritis (GN) by posttransplant serum 25-hydroxyvitamin D (25[OH]D) levels in overall study population. Adjusted for recipient age at transplant, sex, race, donor status, prior kidney transplant, measurement time of 25(OH)D.

recurrence (subdistribution HR: 5.26; 95% CI, 1.63-16.95) compared with vitamin D sufficiency. We did not detect significant associations between 25(OH)D and the recurrence of IgAN. Results did not change significantly after further adjusting for concurrent measurements of UPCR, serum albumin, and serum creatinine. Stratified analyses were infeasible in other GNs because of the limited sample size.

Sensitivity Analyses

Excluding the first month after 25(OH)D measurement from the period at risk also did not substantially change the estimated association of 25(OH)D with recurrence in the overall study population (Table S2, **SDC**, http://links.lww.com/TXD/A627). Similarly, a stronger association remained in recipients with FSGS in the overall study population (Table S3, **SDC**, http://links.lww.com/TXD/A627). The overall association remained significant in analyses excluding the first month after 25(OH)D measurement and further adjusting for concurrent UPCR, serum albumin, and eGFR (Table S4, **SDC**, http://links.lww.com/TXD/A627).

DISCUSSION

Recurrence remains an unsolved problem in KTRs with ESKD due to GN. There is no proven strategy to prevent GN recurrence given our incomplete understanding of its pathophysiology.[28] Results are controversial for potential risk factors proposed in previous research.[4,8-10] We found that lower posttransplant serum 25(OH)D level was associated with a higher hazard of recurrence after adjustment for relevant potential confounders. We observed an approximately linear relationship between serum 25(OH)D and GN recurrence. These results suggest that the current threshold of vitamin D sufficiency (ie, 30 ng/mL) proposed in the general population may not be optimal in KTRs. The majority of recurrence captured in this study was relatively late (median: 4.6 y; IQR: [0.9–8.7]) as expected given the requirement for posttransplant 25(OH)D measurement. These findings highlight the need to study vitamin D deficiency as a modifiable risk factor for late GN recurrence as allograft survival increases further. Although we did not have adequate statistical power to detect quantitative differences across different GNs, we detected stronger associations in FSGS.

It is expected that recipients with disease recurrence would have lower levels of circulating 25(OH)D compared with those without recurrence as a result of proteinuria and impaired vitamin D metabolism after recurrence.[29-31] We observed the relationship between circulating 25(OH)D and UPCR, serum albumin, and eGFR as expected. However, serum 25(OH)D analyzed in this study was measured several

TABLE 3.

Association between posttransplant 25(OH)D and recurrence of specific GN

Primary GN		Sample size	Serum 25(OH)D	Subdistribution HR (95% CI)[a]
Focal segmental glomerulosclerosis	Primary analyses[b]	270 KTRs (20 events)	Per ng/mL lower	1.08 (1.03-1.12)
			Sufficiency (≥30 ng/mL)	Reference
			Insufficiency (21–29 ng/mL)	2.38 (0.72-7.89)
			Deficiency (≤20 ng/mL)	5.26 (1.63-16.95)
	Secondary analyses[c]	221 KTRs (16 events)	Per ng/mL lower	1.09 (1.02-1.16)
			Sufficiency (≥30 ng/mL)	Reference
			Insufficiency (21–29 ng/mL)	1.29 (0.19-8.84)
			Deficiency (≤20 ng/mL)	7.47 (2.18-25.65)
IgA nephropathy	Primary analyses[b]	315 KTRs (26 events)	Per ng/mL lower	1.01 (0.97-1.05)
			Sufficiency (≥30 ng/mL)	Reference
			Insufficiency (21–29 ng/mL)	0.85 (0.31-2.31)
			Deficiency (≤20 ng/mL)	2.16 (0.85-5.51)
	Secondary analyses[c]	239 KTRs (18 events)	Per ng/mL lower	0.99 (0.96-1.03)
			Sufficiency (≥30 ng/mL)	Reference
			Insufficiency (21–29 ng/mL)	0.57 (0.17-2.00)
			Deficiency (≤20 ng/mL)	1.04 (0.32-3.36)

Subgroup analysis was infeasible in other GNs due to limited sample size. Competing risk regression models were fitted with allograft failure due to other causes (including death) as competing events. One year after each serum 25(OH)D measurement was regarded as a period at risk.

[a]Models were adjusted for recipient age at transplant and measurement time of 25(OH)D (ie, months after transplant) in primary analyses; models were further adjusted for concurrent urine protein–creatinine ratio (UPCR), serum albumin, and estimated glomerular filtration rate (eGFR) in secondary analyses.

[b]Primary analyses were conducted in the total study population.

[c]Secondary analyses were conducted in the study population where concurrent measurements of UPCR, serum albumin, and serum creatinine were available.

25(OH)D, 25-hydroxy vitamin D; GN, glomerulonephritis; HR, hazard ratio; CI, confidence interval; KTR, kidney transplant recipient.

months to years before the diagnosis of recurrence. The association of circulating 25(OH)D and recurrence did not significantly change after further adjusting for concurrent UPCR, serum albumin, and eGFR where available in secondary analyses. Similarly, results were relatively unchanged in analyses excluding the first month after 25(OH)D measurements.

Laboratory studies have found that 1,25-dihydroxyvitamin D, the biologically active form of vitamin D, could modulate the differentiation of antigen-presenting cells to favor immunotolerance,[32] suppress T lymphocyte proliferation, modulate differentiation of different T cells,[33] and inhibit the production of immunoglobin.[34] In addition to its properties in immunoregulation, vitamin D also demonstrates anti-inflammatory,[35] anti-proliferation,[36] and podocyte preservation[37,38] effects in experimental models of GN. These findings provide potential pathways for the observed association of circulating 25(OH)D and GN recurrence.[13] The metabolism of vitamin D is complex in KTRs, with simultaneous secondary hyperparathyroidism and long-term exposure to immunosuppressants. The immune properties of vitamin D might be modified in this immunocompromised population. Furthermore, GN is a heterogeneous mixture of various glomerular diseases. The observed stronger association of circulating 25(OH)D and recurrence in FSGS might indicate distinct effects of vitamin D on the pathogenesis of recurrence in specific GN diseases. More in-depth research on immunoregulation of vitamin D in KTRs and specific GN diseases is required. Evidence from observational studies has revealed that vitamin D deficiency is associated with a higher incidence and more severe disease activity of rheumatoid arthritis,[39] systemic lupus erythematosus,[40] and multiple sclerosis in nontransplant populations.[41] Vitamin D and omega 3 trial (VITALE), a nationwide randomized controlled trial,[42] recently found that vitamin D supplementation for 5 y reduced incident autoimmune disease by 22%. It is currently unknown whether this association extends to other autoimmune and inflammatory diseases. Clinical trials and additional observational studies in KTRs are needed to provide evidence to determine whether there is a causal relationship between 25(OH)D and GN recurrence.

There are several strengths of our study. Foremost, we used updated posttransplant serum 25(OH)D measurement instead of only 1 measurement at a specific time before or after transplant. Levels of circulating vitamin D commonly do not fully recover after a successful kidney transplantation.[24,43] It is also affected by persistent exposure to immunosuppression and limited sunshine exposure after transplant. On the other hand, vitamin D deficiency could be improved via supplementation. Regarding posttransplant serum 25(OH)D level as a time-varying covariate more accurately presents the actual vitamin D status across years after transplantation than a single measurement. Second, the long-term follow-up of KTRs at our center enabled us to identify late cases of recurrence. The Australia and New Zealand Dialysis and Transplant Registry,[4] a large international registry, found that MPGN and MN bear the highest risk of recurrence, followed by IgAN and FSGS in KTRs followed for a median of 7.7 y. We found similar relative recurrence rates across different GNs in our study population, whereas the overall incidence of recurrence was lower in our study, due at least in part to excluding follow-up time before the first 25(OH)D measurement.

Our study also has several limitations. The problematic diagnosis of GN recurrence is one of the major obstacles confronted by most studies.[10] The incidence of GN recurrence was likely to be underestimated in our study considering eligibility criteria and a clinically driven allograft biopsy policy. Some early cases of recurrence also were excluded if they occurred before the first posttransplant 25(OH)D measurement. This may have further reduced the observed recurrence rate. We suspect a mix of primary, secondary, and genetic FSGS in our study population, presumably resulting in a lower incidence of recurrence of FSGS compared with other registries with mainly primary FSGS.[4,8] Recipients without any valid posttransplant 25(OH)D measurement were excluded from the analysis, which might induce some selection bias. Early recurrent GN might be excluded, especially for FSGS. We found that recipients without valid posttransplant serum 25(OH)D measurement were more likely to have FSGS as the cause of ESKD and have previous kidney transplants (Table S5, **SDC**, http://links.lww.com/TXD/A627). Reversal causality is another concern in our study where posttransplant 25(OH)D was analyzed as a time-varying covariate. We attempted to minimize this by excluding the first month after 25(OH)D measurement from the period at risk in the sensitivity analysis. We also acknowledge the potential for residual confounding in an observational study setting, considering that pathophysiology and relevant risk factors of GN recurrence have not been well-identified.

Despite these limitations, our study highlights the potential relevance of circulating 25(OH)D in the susceptible population of KTR with ESKD due to GN. More studies are needed to further explore the potential roles of vitamin D in the pathophysiology of GN and its recurrence. More evidence from both observational studies and clinical trials is needed to determine the causal relationship between circulating 25(OH)D and GN recurrence.

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