Adverse outcomes associated with IgA Nephropathy (IgAN) recurrence in kidney transplant recipients.

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INTRODUCTION

- Immunoglobulin A nephropathy (IgAN) is the leading cause of glomerulonephritis worldwide and affected individuals have a high lifetime risk of end-stage kidney disease (ESKD).
- Kidney transplantation is the preferred option for IgAN patients who progress to ESKD, However, a previous study reported a 23% IgAN recurrence rate in the transplanted kidney and a 3.7-fold increase in graft rejection in patients with IgAN recurrence.
- Diagnosis of IgAN is challenging as it necessitates a renal biopsy. However, biopsy data is not readily available.

HYPOTHESIS

- Leveraging real-world patient data from electronic medical records (EMRs) across multiple healthcare organizations and the ability to propensity-score match patients on clinical characteristics, we hypothesized that IgAN recurrence would be associated with increased graft failure risk.

METHODS

- TriNetX was used to perform a propensity-score matched study of outcomes in kidney transplant recipients (KTRs) with IgAN as the primary reason for kidney transplantation (12/31/2010 - 12/31/2024).
- Exposures and outcomes of interest were defined using composite ICD and CPT codes.
  - Cohorts were matched based on age, sex, race, ethnicity, BMI, and donor status.
  - Outcomes of interest included IgAN recurrence, kidney transplant rejection, and cytomegalovirus (CMV) infection post-transplant.
  - Cox regression was used to evaluate the outcomes.

RESULTS
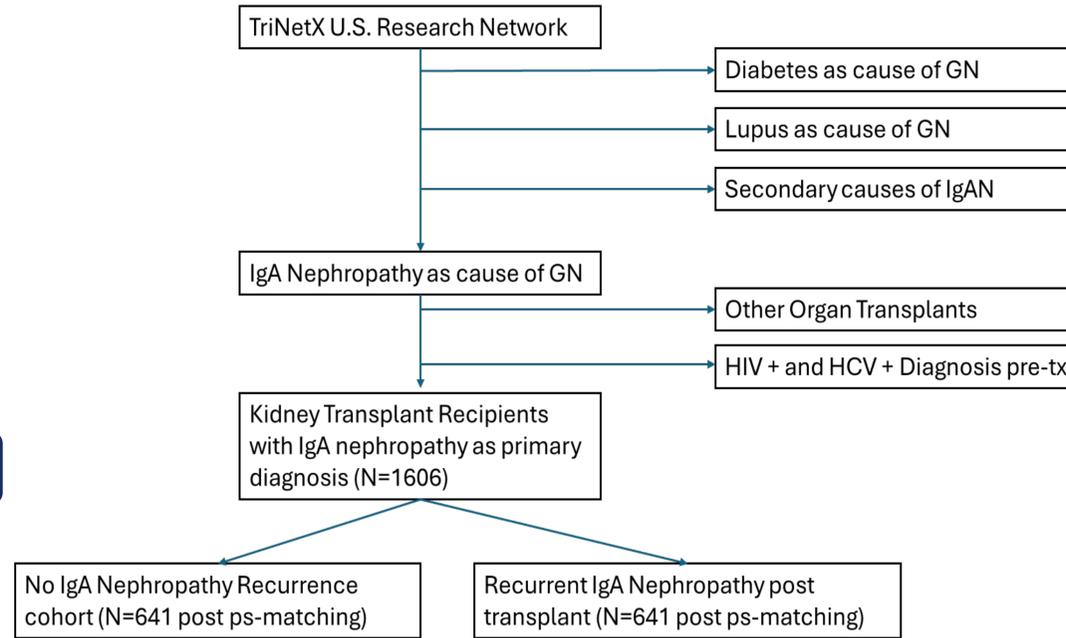
Figure 1: Cohort design for the TrinetX study. Our initial cohort narrowed the database network to adult, viral hepatitis-/HIV-, first-time renal transplant-only recipients with IgA nephropathy as the primary diagnosis for transplant. The sub-cohorts were defined based on the recurrence of IgA nephropathy within the 1st year post-transplant and followed for 5 years for outcomes of interest.

Table 1. Demographic characteristics of study participants pre and post propensity score matching

Patient Characteristics	Before Matching			After Matching		
	Mean ± SD; n (%)			Mean ± SD; n (%)		
	IgA Recurrence (n=817)	No IgA Recurrence (n=758)	p-value	IgA Recurrence (n=641)	No IgA Recurrence (n=641)	p-value
Age at Index (yrs)	45.69 ± 13.55	47.90 ± 14.53	<0.05	47.00 ± 13.65	46.70 ± 14.43	0.71
Black or African American	50 (6.12%)	62 (8.18%)	0.11	42 (6.55%)	46 (7.18%)	0.8
Male	491 (60.10%)	457 (60.29%)	0.94	394 (61.47%)	381 (59.44%)	0.46
Living Donor	299 (36.60%)	190 (25.07%)	<0.05	189 (29.48%)	187 (29.17%)	0.9
BMI ≥ 25 kg/m²	512 (62.67%)	464 (61.21%)	0.55	401 (62.56%)	407 (63.49%)	0.73
eGFR ≤ 30 mL/min/1.73 m²	786 (96.21%)	726 (95.78%)	0.66	620 (96.72%)	616 (96.1%)	0.55
CMV infections				199 (30.43%)	150 (22.94%)	
Kidney transplant rejections				279 (42.66%)	253 (38.68%)	

*The p-value was calculated using a t-test for continuous variables and a chi-square test for categorical variables. CMV infections and kidney transplant rejections were determined using composite logical observation identifier names and codes (LOINC) as well as ICD-10 codes.
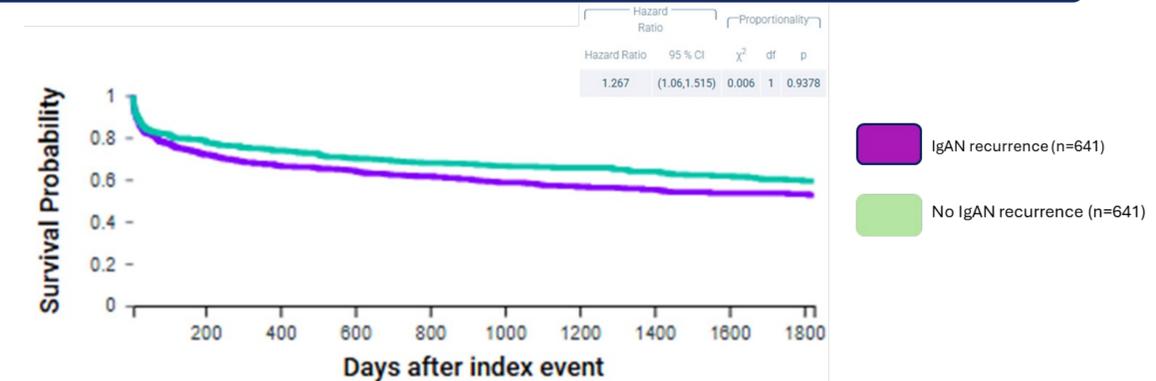
Figure 2: Kaplan-Meier curves for rejection free survival associated with IgAN recurrence over 5 years of follow up among kidney transplant recipients with IgA nephropathy (IgAN). Cohorts were matched based on age, sex, race, ethnicity, BMI, and donor status.
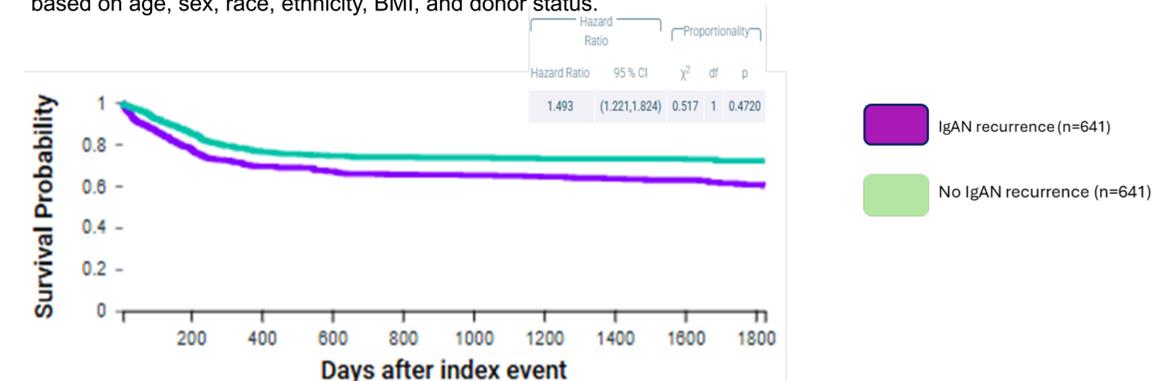
Figure 3: Kaplan-Meier curves for infection free survival associated with IgAN recurrence over 5 years of follow up among kidney transplant recipients with IgA nephropathy (IgAN). Cohorts were matched based on age, sex, race, ethnicity, BMI, and donor status.

- KTRs with IgAN recurrence had 1.27 times greater risk of transplant rejection (95% CI: 1.06-1.51) and 1.49 times greater risk of CMV infection (95% CI: 1.06-1.51) compared to those without recurrence.

CONCLUSIONS

- Our study found that KTRs with IgAN recurrence in the TrinetX database had significantly greater risk of rejection and CMV infection post-transplant.
- Despite limitations in the generalizability of EMR data, this represents an opportunity for further insight into differences in the early post-transplant period to identify modifiable risk factors associated with IgAN recurrence in KTRs