Association of Subclinical Kidney Transplant Rejection with 10-Year All Cause Graft Loss
An Analysis of the CTOT-08 Study

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BACKGROUND

Kidney transplant (KTx) is the treatment of choice for ESKD

Drastic reductions in first-year allograft rejection rates have not appreciably improved graft half-life, and 10-20% of KTx annually are for failed allografts

Nearly half of graft losses after 1-year post-transplant are due to acute and chronic rejection

Subclinical rejection (SubAR) has been associated with worse allograft outcomes at 2 years, but associations with long-term graft survival are lacking

METHODS

Long-term follow-up analysis of multicenter 24-month observational data (CTOT-08)

Subjects: CTOT-08 subjects able to be matched to 10-year SRTR patient outcomes and validated by clinical sites

Definitions:

All Cause Graft Loss (ACGL): Patient death with a functioning allograft or death-censored allograft loss

Statistical Analyses:

Kaplan Meier method to compare univariate event-free survival rates between cohorts

Time-dependent Cox Model used to model association between time to ACGL accounting for potential confounders. Stepwise variable selection approach used to fit the best model (0.25 entry criterion, 0.15 criterion to remain)

Planned variables: Black race, sex, DM as cause of ESKD, living donor transplant, depleting induction at time of transplant, donor age, clinical acute rejection, subAR as a time-varying covariate

RESULTS

Table 1. Patient Demographics and Transplant Characteristics

	All (N=276)	No SubAR (N=165)	1 SubAR (N=87)	>1 SubAR (N=24)
Recipient Age	52 ± 14	52 ± 14	52 ± 14	52 ± 12
Gender				
Male	179 (65%)	104 (63%)	59 (68%)	16 (67%)
Female	97 (35%)	61 (37%)	28 (32%)	8 (33%)
Race				
Black/African American	54 (20%)	32 (19%)	17 (20%)	5 (21%)
White	177 (64%)	106 (64%)	55 (63%)	16 (67%)
Asian	11 (4%)	11 (7%)	0 (0%)	0 (0%)
Native American/Alaskan	5 (2%)	1 (1%)	3 (3%)	1 (4%)
Pacific Islander	3 (1%)	1 (1%)	1 (1%)	1 (4%)
More than One Race	2 (1%)	1 (1%)	1 (1%)	1 (4%)
Unknown/Not Reported	24 (9%)	13 (8%)	10 (11%)	1 (5%)
Cause of ESKD				
Cystic	36 (13%)	24 (15%)	7 (8%)	5 (21%)
Diabetes Mellitus	56 (20%)	32 (19%)	20 (23%)	4 (17%)
Glomerulonephritis	75 (27%)	50 (30%)	17 (20%)	8 (33%)
Hypertension	45 (16%)	26 (16%)	17 (20%)	2 (8%)
Other	64 (23%)	33 (20%)	26 (30%)	5 (21%)
Donor Age	41 ± 14	41 ± 14	41 ± 15	38 ± 12
cPRA	4 [0,60]	3 [0,53]	5 [0,64]	34 [0,84]
Living Donor	152 (55%)	103 (62%)	38 (44%)	11 (46%)
Deceased Donor	124 (45%)	62 (38%)	49 (56%)	13 (54%)
Induction				
Anti-thymocyte globulin	71 (26%)	41 (25%)	24 (28%)	6 (25%)
Alemtuzumab-1H	142 (51%)	83 (50%)	44 (51%)	15 (63%)
Basiliximab	56 (20%)	34 (21%)	20 (23%)	2 (8%)
Maintenance Immunosuppression				
Tacrolimus	275 (100%)	164 (99%)	87 (100%)	24 (100%)
Mycophenolate	274 (99%)	165 (100%)	85 (100%)	24 (100%)
Steroids	167 (61%)	87 (53%)	61 (70%)	19 (80%)
Belatacept	2 (1%)	2 (1%)	0 (0%)	0 (0%)

Table 2. All Cause Graft Loss Between Cohorts

Group	All Cause Graft Loss
No SubAR	43 (26%)
1 SubAR	27 (31%)
>1 SubAR	10 (42%)

Table 3. Surveillance Biopsy Diagnoses by Time Point

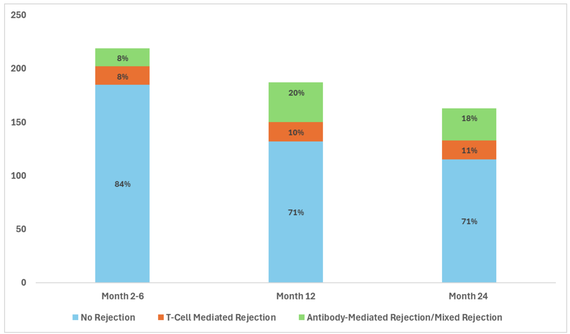
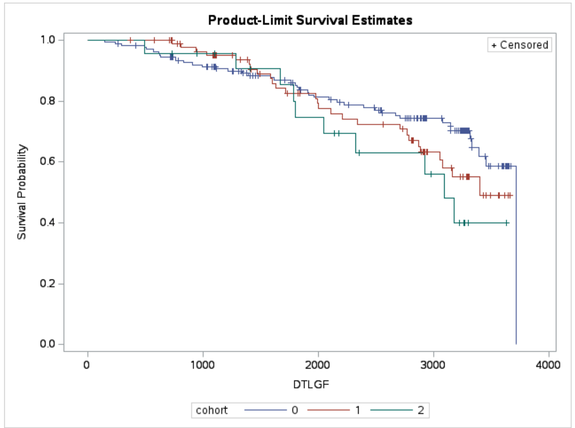


Figure 1. Kaplan Meier Curve



RESULTS

Table 4. Cox Model with Time-Varying Subclinical Rejection

Parameter	aHR	95% CI	P-value
Time-varying Subclinical Rejection	1.67	1.02, 2.74	0.04
Clinical Rejection	2.96	1.04, 8.40	0.04
Living Donor	0.51	0.33, 0.78	<0.01
Donor Age	1.02	1.00, 1.04	0.04
Diabetes	1.49	0.93, 2.39	0.09

CONCLUSIONS

This is the longest multicenter evaluation of prospectively collected subAR on long-term allograft survival

SubAR as a time-varying covariate was strongly and independently associated with ACGL after controlling for potential confounding variables, including the impact of clinical acute rejection

Further analysis to determine if severity of subAR is impactful is warranted

Interventional studies treating subAR to determine the impact on ACGL will be necessary to confirm subAR is a mutable risk factor

REFERENCES

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