Evaluation of Tutivia Biomarker for Risk of Acute Rejection in Patients Experiencing Delayed Graft Function

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Background

oThe incidence of delayed graft function (DGF) in kidney transplant recipients (KTR) is nearly 40%, which can increase the risk of acute rejection (AR). Identifying AR as a cause of persistent DGF is challenging due to a lack of clinical indicators, leading to frequent biopsies. There is a need for reliable early post-transplant biomarkers to rule out rejection and reduce biopsy necessity. This study evaluates the Tutivia RNASeq biomarker test for assessing the risk of acute rejection in patients with DGF.

Methods

Continuous variables are reported as medians with interquartile ranges, and categorical variables as counts with percentages. The demographics of patients who experienced rejection versus those who did not were compared using the Wilcoxon rank-sum test for continuous variables and Fisher's exact test for categorical variables. The Wilcoxon rank-sum test was also used to compare AR scores in patients with biopsy.

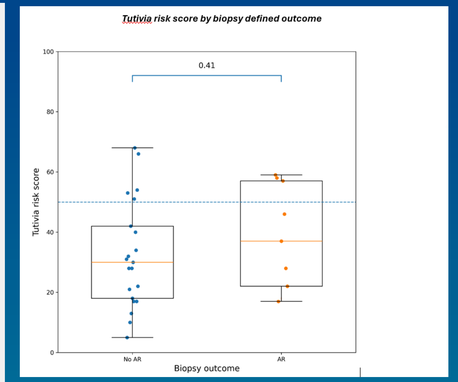
To evaluate the diagnostic performance of the Tutivia risk score for biopsy-proven acute rejection, we analyzed patients who had biopsies during the delayed graft function (DGF) period and a Tutivia measurement within 30 days prior. Scores >50 were considered high risk for rejection, and we calculated sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and odds ratio (OR) for AR. Additionally, the analysis included patients with DGF and Tutivia measurements during that period without biopsies, presumed as no AR. A secondary analysis focused on patients who had biopsies outside the DGF period or lacked a Tutivia measurement within 30 days. Logistic regression assessed the association between Tutivia scores and biopsy-proven AR with longer intervals between measurements and biopsies. Subgroup analyses evaluated the link between Tutivia scores during DGF and AR detected in subsequent biopsies outside that period.

Results

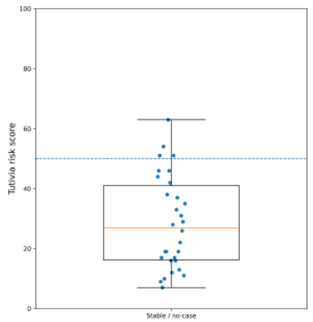
Patient characteristics

Characteristic	Overall N = 45[1]	Group 1 No AR N = 14[1]	Group 1 AR N = 6[1]	Group 1 p-value[2]	Group 2 No AR N = 15[1]	Group 2 AR N = 4[1]	Group 2 p-value[2]
BMI	33.8 (26.9, 36.0)	27.9 (22.9, 39.9)	34.5 (29.8, 35.6)	0.4	32.3 (24.9, 35.6)	33.3 (25.9, 35.7)	>0.9
Race				0.2			0.5
African American	29 (64.4%)	7 (50.0%)	6 (100.0%)		9 (60.0%)	2 (50.0%)	
Asian	2 (4.4%)	1 (7.1%)	0 (0.0%)		1 (6.7%)	0 (0.0%)	
Caucasian	3 (6.7%)	1 (7.1%)	0 (0.0%)		0 (0.0%)	1 (25.0%)	
Hispanic	11 (24.4%)	5 (35.7%)	0 (0.0%)		5 (33.3%)	1 (25.0%)	
Age at transplant	55.0 (48.0, 58.0)	52.0 (46.0, 67.0)	53.5 (31.0, 58.0)	0.6	55.0 (48.0, 57.0)	51.5 (44.0, 54.0)	0.3
Legal sex				>0.9			0.3
Female	14 (31.1%)	5 (35.7%)	2 (33.3%)		3 (20.0%)	2 (50.0%)	
Male	31 (68.9%)	9 (64.3%)	4 (66.7%)		12 (80.0%)	2 (50.0%)	
Multiorgan transplant	2 (4.4%)	0 (0.0%)	1 (16.7%)	0.3	1 (6.7%)	0 (0.0%)	>0.9
DDKT	45 (100.0%)	14 (100.0%)	6 (100.0%)	>0.9	15 (100.0%)	4 (100.0%)	>0.9
PRA class I	6.0 (0.0, 48.0)	8.5 (2.0, 57.0)	6.5 (0.0, 18.0)	0.4	7.0 (0.0, 65.0)	22.5 (7.5, 44.0)	0.7
PRA class II	17.0 (0.0, 45.0)	32.0 (3.0, 60.0)	22.5 (16.0, 45.0)	0.9	9.0 (0.0, 28.0)	27.0 (13.0, 55.5)	0.5
KDPI	60.5 (44.5, 77.0)	76.0 (54.0, 86.0)	58.5 (42.0, 75.0)	0.2	62.0 (47.0, 77.0)	59.5 (48.5, 76.5)	>0.9

Tutivia risk score by biopsy defined outcome



Tutivia risk score in DGF patients without biopsy

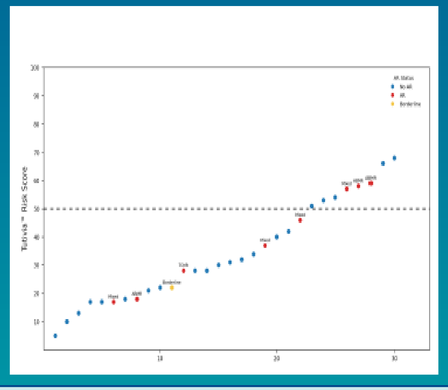


Biopsy Group	AR	No AR	Total
Risk score > 50	3	5	8
Risk score ≤ 50	5	16	21
Total	8	21	29

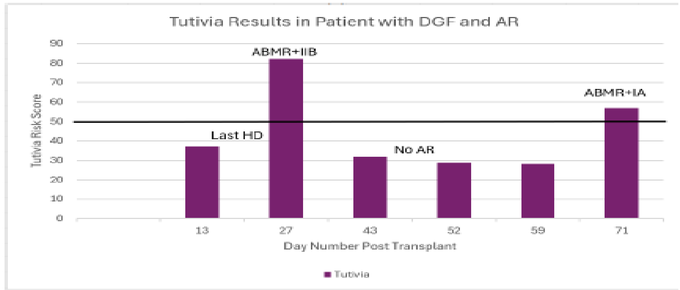
Overall DGF Group	AR	No AR	Total
Risk score > 50	3	9	12
Risk score ≤ 50	5	42	47
Total	8	51	59

Performance metric	Performance (%) In biopsy patients	Performance (%) In all DGF patients
Sensitivity	37.5	37.5
Specificity	76.2	82.4
PPV	37.5	25.0
NPV	76.2	89.4
PPV (adjusted to 20% prevalence)	28.3	34.7
NPV (adjusted to 20% prevalence)	83.0	84.1
Odds ratio	1.92	2.8

Diagnostic performance of Tutivia with for biopsy-proven rejection (threshold = 50)



Biopsy results from 3 separate biopsies are labeled with histopathology findings; HD (Hemodialysis)



Conclusion

Tutivia performance demonstrated a high NPV during episodes of DGF when other clinical indicators are limited. The high NPV may guide clinicians in decisions regarding need to perform a biopsy to rule out AR and may assist in guiding immunosuppression management during DGF episodes with serial Tutivia monitoring. Further analysis is needed to better validate its role in predicting acute rejection and long-term renal allograft function

Conflict of interest : Speaker , advisor Vericidx, Natera

References

Bestard O, Augustine J, Wee A, Poggio E, Mannon RB, Ansari MJ, Bhati C, Maluf D, Benken S, Leca N, La Manna G, Samaniego-Picota M, Shawar S, Concepcion BP, Rostaing L, Alberici F, O'Connell P, Chang A, Salem F, Kattan MW, Gallon L, Donovan MJ. Prospective observational study to validate a next-generation sequencing blood RNA signature to predict early kidney transplant rejection. Am J Transplant. 2024Mar;24(3):436-447 doi: 10.1016/j.ajt.2023.09.021. Epub 2023 Dec 7. PMID: 38152017.