In vivo assessment of interstitial fibrosis and tubular atrophy (IFTA) and inflammation in renal allografts using multi-wave quantitative ultrasound

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Background, motivation and objective

Renal transplant is the preferred long-term treatment for end-stage renal disease. The most common cause of chronic transplant rejection is interstitial fibrosis and tubular atrophy (IFTA), which in turn is the endpoint of chronic active inflammation. Graft surveillance is typically performed using surrogates of kidney function, which is not efficient for early detection of rejection. In a previous study, we showed preliminary results of interstitial fibrosis diagnosis using multi-wave quantitative ultrasound (MWQUS) in 22 transplant recipients. The present study reports results with an extended cohort of 69 recipients and explores the relationship of MWQUS with IFTA and inflammation assessed from protocol biopsy.

Statement of Contribution/Methods

MWQUS parameters were estimated using a GE Logiq E9 scanner with a C1-6-D transducer operating in Comb-push Ultrasound Shear Elastography mode. Biopsy results indicated 34 grafts had neither IFTA nor inflammation (No-IFTA|i group) and 35 had either IFTA or inflammation (IFTA|i group) (27 IFTA only, 4 inflammation only, and 4 IFTA and inflammation). Two ultrasound parameters (i.e., average backscatter coefficient (aBSC) and shear wave speed (SWS)), one renal function surrogate (i.e., estimated glomerular filtration rate (eGFR)) and the time from transplant to biopsy (TTB) were analyzed. Parameters were compared using two-sided Wilcoxon rank sum test and classification between the (No-IFTA|i) and (IFTA|i) groups was performed using logistic regression with the operating point in the ROC curve maximizing Youden's index.

Results/Discussion

When compared to the No-IFTA|i group, the aBSC exhibited a significant increase ($p<0.05$) in the presence of IFTA alone, inflammation alone, and IFTA with inflammation. No other parameter exhibited statistically significant difference between healthy and diseased grafts. The regression model that uses aBSC alone obtained 0.78 accuracy and 0.85 area under the curve (AUC) when differentiating between the No-IFTA|i and IFTA|i groups. The addition of SWS and TTB increased both accuracy (0.84) and AUC (0.90). In contrast, the use of eGFR alone resulted in 0.58 accuracy and 0.57 AUC. These results suggest that MWQUS is sensitive to the presence of both inflammation and IFTA, and may outperform currently available blood test markers when assessing the onset of chronic graft rejection.

	aBSC	aBSC + SWS	aBSC + SWS + TTB	eGFR
Sensitivity	0.66	0.83	0.91	0.26
Specificity	0.91	0.82	0.77	0.91
Accuracy	0.78	0.83	0.84	0.58
AUC	0.86	0.87	0.90	0.57

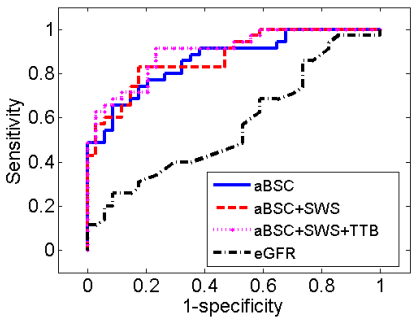

Fig. Classification of healthy transplants vs. transplants with either inflammation or IFTA. Left: Classifier performance using (i) aBSC, (ii) aBSC and SWS, (iii) aBSC, SWS and TTB, and (iv) eGFR. Right: ROCs corresponding to each classifier.