Arterial Spin Labeling and Blood Oxygen Level-Dependent Imaging for the Assessment of Tissue Oxygenation and Perfusion in Kidney Allografts

To the Editor: We read with great interest and congratulate the recently published article by Prasad *et al.*[1] that corroborated the tissue hypoxia hypothesis in human chronic kidney disease by using quantitative blood-oxygen level dependent (BOLD) imaging and ferumoxytol to measure tissue oxygenation and fractional blood volume, respectively. We are curious to evaluate the oxygenation and perfusion status in kidney allografts with recurrent/*de novo* glomerulonephritides.

A retrospective analysis of prospectively acquired data was performed in 10 allografts with biopsy-proven glomerulonephritides (study group) and 9 age- and sex-matched apparently healthy kidney transplants (control group). All the included patients underwent BOLD and arterial spin labeling (ASL) imaging between July 2017 and July 2018, and the detailed imaging protocols and parameters were the same as we reported previously.[2] Cortical and medullary oxygenation (indicated by the R2*) and cortical perfusion were obtained from BOLD and ASL, respectively, by applying the region-of-interest method. Patient demographics, laboratory measurements, and imaging results were presented in Table 1. The median estimated glomerular filtration rate of the study group was approximately one-third of the control group, and cortical perfusion in the former group was significantly lower than that in the control group ($P < 0.001$). Notably, both cortical and medullary R2* in the study group had no statistical difference with those of the control group (both $P > 0.05$). Correlation analysis (Supplementary Figure S1) indicated that hematocrit was significantly inversely correlated with cortical R2* ($\rho = -0.58$, $P = 0.009$), but not

Table 1. Patient demographics, laboratory measurements, and imaging results

Variables	Control group ($n = 9$)	Study group ($n = 10$)	*P* value
Clinical characteristics			
Age (yr)	35 ± 9	37 ± 9	0.55
Sex (male: female)	7:2	8:2	0.91
Allograft age (mo)	10 (6–15)	25 (12–34)	0.07
Causes for ESKD (*n*, %)			0.28
Unknown (*n*, %)	6 (67)	8 (80)	
Glomerulonephritides (*n*, %)	1 (11)	2 (20)	
Other (*n*, %)	2 (22)	0 (0)	
Kidney transplant type (*n*, %)			0.81
Living-related	5 (56)	5 (50)	
Deceased	4 (44)	5 (50)	
Immunosuppressive regimen (*n*, %)			0.30
Pre + Tac + MMF	8 (89)	6 (60)	
Other	1 (11)	4 (40)	
Laboratory measurements			
Serum creatinine (mg/dl)	1.30 ± 0.21	2.93 ± 1.09	0.001
eGFR (ml/min per 1.73 m^2)	67 (62–75)	22 (17–53)	<0.001
Proteinuria (g/24 h)	0.30 (0.18–0.51)	1.50 (0.44–9.86)	0.01
Hematocrit	0.390 ± 0.066	0.351 ± 0.065	0.21
Hemoglobin (g/l)	126 ± 23	113 ± 24	0.27
Albumin (g/l)	44.99 ± 5.00	33.71 ± 8.83	0.004
Imaging findings			
Cortical R2* (Hz)	16.72 (15.33–20.75)	19.14 (16.03–22.74)	0.24
Medullary R2* (Hz)	30.19 (27.95–33.30)	30.13 (27.45–32.24)	0.78
Cortical ASL (ml/min per 100 g)	150.61 (85.57–192.00)	65.38 (43.14–84.11)	0.01

ASL, arterial spin labeling; eGFR, estimated glomerular filtration rate, as calculated using the Chronic Kidney Disease Epidemiology Collaboration equation; ESKD, end-stage kidney disease; MMF, mycophenolate mofetil; Pre, prednisone; Tac, tacrolimus.
Continuous variables with normal distribution were expressed as mean ± SD and compared with the independent Student *t*-test. Continuous variables with non-normal distribution were expressed as median with interquartile range and compared with the Mann-Whitney *U* test. Categorical variables were presented with number (n) and percentage (%) and compared using the chi-square test.

medullary R2*($\rho = -0.01$, $P = 0.96$). The correlations between estimated glomerular filtration rate and cortical R2*, medullary R2*, and cortical ASL were -0.41 ($P = 0.08$), -0.13 ($P = 0.61$), and 0.75 ($P < 0.001$), respectively.

In congruence with prior publications,[3,4] our study revealed that there was a trend toward cortical hypoxia with declining estimated glomerular filtration rate. The current study also supports the hypothesis that hypoxia as measured by BOLD R2* is driven by allograft perfusion. A reduction in perfusion as measured with ASL is probably more meaningful to distinguish between groups of patients with different kidney functions. Since the BOLD technique takes advantage of the paramagnetic/diamagnetic properties of deoxygenated/oxygenated hemoglobin,[5] confounding factors such as hematocrit, oxygen saturation rate, and fractional blood volume should be taken into consideration when interpreting BOLD results. BOLD and ASL were found to have great promise in the noninvasive interrogation of kidney allograft viability in various pathophysiological conditions that could be potentially used for translational researches in the future.

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SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Figure S1. Spearman correlation analysis among hematocrit, estimated glomerular filtration rate, cortical R2* (CR2), medullary R2* (MR2), and cortical arterial spin labeling (ASL) in both the study group and the control group. *, **, and *** indicated $P < 0.05$, <0.01 and <0.001, respectively.

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