Quantification of Renal Lipid and Oxygenation in Diabetic Mice by Magnetic Resonance Imaging

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INTRODUCTION

There is growing evidence that abnormal lipid metabolism and renal accumulation of lipids play a role in pathogenesis of diabetic nephropathy. There is also increasing evidence suggesting an association between chronic renal hypoxia and the development and progression of diabetic nephropathy. Noninvasive quantitative measurements would have major advantages in developing novel treatments that target renal lipid accumulation and hypoxia. The purpose of this study was to study the feasibility of in vivo MR measurement of lipid accumulation and oxygenation in kidney in diabete (*db/db*) mouse model.

METHODS

Chemical shift imaging (CSI) and blood oxygen level-dependent (BOLD) magnetic resonance imaging were performed to measure kidney lipid contents (LC) and dynamic changes of the renal function on the blood-oxygen saturation before and after exposure to pure nitrogen atmosphere and administration of furosemide in *db/db* and wild type (WT) control mice using 7 Tesla scanner. Distribution of visceral and subcutaneous adipose tissue and kidney volume were evaluated by T1-weighted imaging.

RESULTS

Kidney LC in *db/db* mice was significantly higher than that of control group, and lipid accumulation in renal cortex of *db/db* mice was significantly higher than that of renal medulla. Kidney volume and visceral fat ratio to total white adipose tissue (WAT) in *db/db* mice were significantly higher than that of WT mice. Linear correlation was observed between MR measurement method and chemical lipid analysis.The lower baseline T2* values in cortex (CO), outer medulla (OM) and inner medulla (IM) of the diabetic mice indicated lower energy reserve than that of control group. The lower T2* values in CO of diabetic kidney after hypoxia and after injection of furosemide than that of control group, and significant linear correlation between baseline T2* value and lipid content suggested renal hypoxia potentially due to lipid accumulation in cortex.

CONCLUSION

CSI can detect renal lipid accumulation. BOLD imaging is useful to research renal oxygenation. Lower oxygenation of diabetic kidney indicates renal chronic hypoxia, potentially because of lipid accumulation. MRI has potential to longitudinally study renal diseases resulting from lipotoxicity and hypoxia.

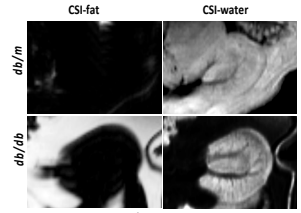


Fig 1. An example of *in vivo* CSI (selective fat and water protons imaging) of *db/db* and WT mouse kidney.

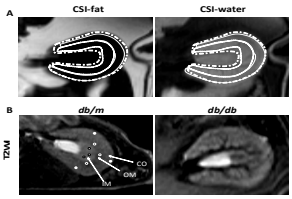
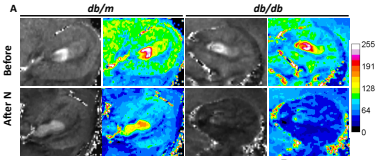


Fig 2. Examples of selection and location of regions of interest for LC and T2* measurements. A: CSI (selective fat and water protons imaging) of kidney; B: T2WI for selecting in BOLD image.



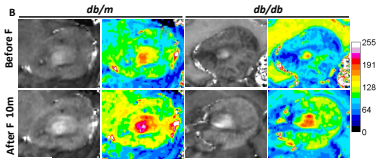


Fig 3. Comparison of the T2*maps of a mouse kidney obtained (**A**) pre- and post-exposure to the pure nitrogen gas and (**B**) pre- and post-injection of furosemide.

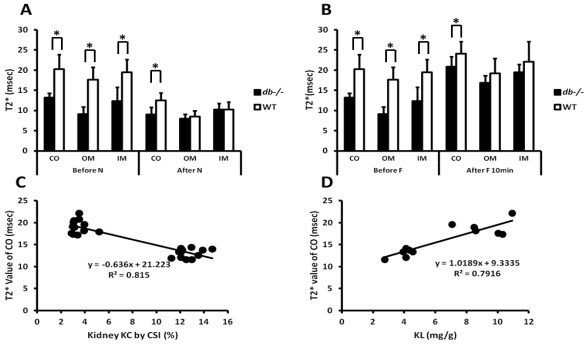


Fig 4. Mean T2* values in CO, OM and IM of db/db mice were significantly lower than that of WT group. In both groups, T2* was significantly lower in OM than in other compartments of kidney. After respiration of pure nitrogen, T2* in CO, OM, and IM decreased by 30–40% in WT mice, and CO of *db/db* mice decreased by 30%. The value of CO in *db/db* mice was significantly lower than that of control group, but T2* signals of OM and IM exhibited no difference between two groups. The infusion of furosemide induced significant increase in T2* comparing that before injection in all compartments of *db/db* group and CO of WT group. The T2* value of CO in *db/db* mice was significantly lower than that of control group, but there were no difference found in the OM and IM between two groups. A significant linear correlation is observed between baseline T2* value of the CO and the FC calculated by the MRI or chemical analysis

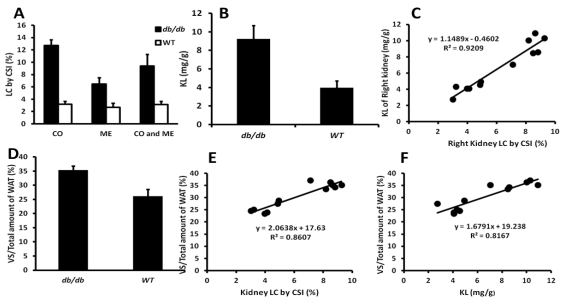


Fig 5. Averaged kidney LC of renal cortex and renal medulla were significantly higher in *db/db* mice than WT mice using CSI, LC in medulla of *db/db* mice is lower than that in renal cortex, but no significant difference between renal cortex and medulla was found in WT mice. The averaged KL in *db/db* mice calculated by chemical analysis method was higher than that of WT mice (A). The whole kidney LC_{CSI} obtained from imaging measurement was higher in *db/db* mice than that of the control group (B). A strong correlation between averaged KL measured by chemical method and LC calculated by MR method was observed (C). Visceral fat of total amount of WAT in *db/db* mice was significantly higher than that of WT mice. A linear correlation is observed between visceral fat of total amount of WAT and LC calculated by MR measurement method or chemical lipid analysis (E, F).

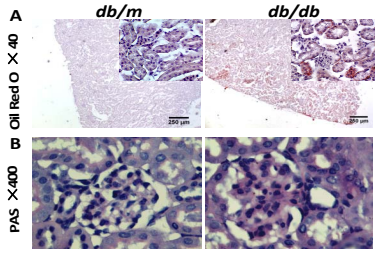


Fig 6. A: Oil Red O staining (×40), inserted boxes show increased magnification of lipid droplets (×400). Lipid deposits are localized mostly within tubular epithelial cells in cortex of *db/db* mice, but are not detectable in WT mice; **B:** Periodic acid Schiff staining (×400). Glomerular injury in the diabetic mice was characterized by the mesangial extracellular matrix expansion and glomerular enlargement. There was significant difference in the glomerular area between db/db and WT mice

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