Published in final edited form as:

Radiology. 2013 December ; 269(3): 625–626. doi:10.1148/radiol.13132179.

Science to Practice: Renal Hypoxia and Fat Deposition in Diabetic Neuropathy—New Insights with Functional Renal MR Imaging

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Summary

Despite being a valuable tool for evaluation of the kidneys, renal magnetic resonance (MR) imaging in clinical practice has been limited to depiction of anatomy and provides little diagnostic information about the health and function of the kidney in patients with chronic kidney disease (CKD) and diabetic nephropathy. In this issue, Peng et al (1) have used two MR imaging methods that go beyond depiction of anatomy to show renal function: renal blood oxygen level–dependent (BOLD) MR imaging, which shows oxygen levels in the kidney, and chemical shift–selective imaging, which shows the relative content of fat in the kidney parenchyma. In a mouse model of diabetes, Peng et al have shown higher fat and lower oxygen levels in kidneys of mice with diabetes than in those of normal controls. These MR imaging methods may help clarify the role of fat deposition and hypoxia in the progression of CKD. As the factors that contribute to the progression of CKD are better understood, ultimately more widespread clinical use for functional renal MR imaging protocols such as renal BOLD and chemical shift–selective imaging may be found to evaluate the severity of CKD and monitor the efficacy of clinical interventions, altering the course of disease progression.

The Setting

The mortality, morbidity, and societal costs of CKD are huge. CKD affects 14% of the population in the United States. People with CKD have a mortality rate 59% higher than those with healthy kidneys and are hospitalized 53% more frequently. When CKD progresses to end-stage renal disease, which affects 600 000 people in the United States, regular treatment with dialysis or kidney transplantation is necessary for survival. The rate of death among patients with end-stage renal disease undergoing dialysis is 6.8–8.2 times that of the general public. Patients with CKD or end-stage renal disease account for 24% of total health care expenditures in the United States (2).

Various causes of kidney disease including diabetes, hypertension, and glomerulonephritis converge on the common pathway of CKD. Hypoxia is thought to be an important factor in

Disclosures of Conflicts of Interest: G.R.M. No relevant conflicts of interest to disclose. J.L.Z. No relevant conflicts of interest to disclose. V.S.L. No relevant conflicts of interest to disclose.

the progression of CKD to end-stage renal disease (3). As CKD worsens, the number of capillaries in the peritubular capillary bed in the renal medulla decreases, resulting in decreased medullary oxygen tension. This contributes to the activation of a complex array of cytokines and other factors leading to tubulointerstitial fibrosis and impaired renal function, which are the hallmarks of CKD.

Abnormal deposition of fat is seen at histologic examination of diseased kidneys. A wealth of recent research shows that ectopic fat deposition in solid organs such as the liver and kidneys is not just a sign of disease, but also part of the cause. Adipocytes and adipose-associated tissues and cells such as macrophages do more than just store fat. They also secrete numerous hormones, enzymes, adipokines (peptides), and a wide array of cytokines, many of which affect insulin sensitivity and lipid metabolism. Excess free fatty acids and abnormal deposition of lipids lead to chronic cellular damage known as lipotoxicity (4,5).

The Science

Peng et al (1) studied the kidneys of mice with diabetes by using noninvasive renal BOLD MR imaging and chemical shift-selective imaging to depict renal oxygenation levels and fat content. Renal BOLD MR imaging (6) consists of mapping the T2* relaxation rate by acquiring a series of echoes in a gradient-recalled-echo sequence. Deoxyhemoglobin shortens T2*. Changes in tissue oxygen tension cause changes in deoxyhemoglobin concentration that are manifested on renal BOLD images as changes in T2*. Chemical shift-selective imaging is a method by which frequency-selective pulses (7) are used to excite only fat or only water selectively. The ratio of signal intensity in fat-only and water-only images conveys information about relative fat content. With chemical shift-selective imaging, Peng et al showed that renal cortical fat is increased in kidneys of mice with diabetes. This finding was validated by means of postmortem chemical analysis. They also showed decreased T2* in the kidneys of mice with diabetes with renal BOLD MR imaging, suggesting greater levels of chronic hypoxia in the kidneys of those with diabetes than in normal kidneys (Fig 4a). Quantification of tissue parameters such as lipid content or oxygen levels with MR imaging is difficult because many factors contribute to MR imaging signal intensity. For instance, fat has a short T2*, and fat in the renal cortex may account for some of the T2* decrease attributed to hypoxia in the kidneys of mice with diabetes. Similarly, signal intensity on chemical shift-selective images is affected by variations in radiofrequency field strength and main field strength, potentially affecting the accuracy of fat quantification. Nevertheless, the results presented by Peng et al are encouraging and broaden the scope of functional kidney imaging to emphasize fat quantification.

The Practice

Clinical indications for renal BOLD MR imaging and estimation of fat content with MR imaging are not yet established. Further research is necessary to develop methods for accurate quantification of oxygen levels and fat volume based on MR signal intensity. However, if estimation of renal tissue oxygen tension proves feasible, this noninvasive test could become important in laboratory and clinical trials currently underway that focus on renal hypoxia. These include studies of the administration of vascular endothelial growth

factor, pharmacologic agents that can prolong the half-life of hypoxia-inducible factors in the kidney, and stem cell therapy. Similarly, if lipid levels measurable with MR imaging are proved to be significantly correlated with the severity of CKD, this test could also become a useful clinical tool for evaluation of CKD and its progression. The work presented by Peng et al (1) in this issue is a welcome contribution to our understanding of renal hypoxia and fat deposition and brings us closer to clinically useful, noninvasive renal MR imaging that goes beyond depiction of anatomy to show renal health and function.

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