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Commentary

Role of Renal Sinus Adipose Tissue in Obesity-induced Renal Injury

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The epidemic of obesity and overweight has been reaching unimaginable proportions, and is currently affecting more than 2.1 billion people worldwide (Ng et al., 2014). Obesity is characterized by ectopic fat accumulation, the presence of adipose tissue within tissues that under normal conditions either do not contain or contain small amounts of adipose tissue. Importantly, accumulation of ectopic fat attributed to obesity plays an important role in the development of cardiovascular and metabolic disorders, including diabetes and hypertension (Sironi et al., 2011).

Previous studies have shown that ectopic fat accumulation in the renal sinus (RS) — a compartment located at the medial border of the kidney that contains renal vessels, calices, nerve tissue, and lymphatic channels — is associated with an increased risk of hypertension and chronic renal disease. For example, quantification of RS fat accumulation in participants from the Framingham Heart Study revealed that the amount of RS fat was independently associated with measures of blood pressure and renal function (Foster et al., 2011). Similarly, RS fat accumulation correlated with the number of antihypertensive drugs and blood pressure levels after therapy in individuals at risk for cardiovascular events (Chughtai et al., 2010), suggesting a potential role of this fat depot in hypertension and renal dysfunction. Alas, little is known about the precise mechanism by which RS adipose tissue contributes to renal injury.

In this issue of EBioMedicine, the study of Krievina et al. takes a step in this direction by linking accumulation of adipose tissue in the RS with early diagnostic biomarkers of kidney injury (Krievina et al., in this issue). In this cross-sectional study, 280 asymptomatic middle-age participants were recruited, abdominal and RS adipose tissue were quantified by computed tomography, and serum levels of kidney injury molecule (sKIM)-1 and fibroblast growth factor (FGF)-21 were measured by standard procedures. In addition, 40 subjects from the cross-sectional study group were prospectively followed over a 1-year period. They found that adipose tissue preferentially accumulated in the left RS and was related with retroperitoneal, intraperitoneal, and subcutaneous adipose tissue measurements. Furthermore, RS adipose tissue directly correlated with the early renal injury markers sKIM-1 and FGF-21. Follow up studies showed that accumulation of adipose tissue in the RS was associated with increased visceral adipose tissue volume, whereas reductions in visceral adipose tissue volume were not accompanied by reductions in RS adiposity. Therefore, these observations point to an emerging central role of RS adipose tissue in the development of obesity-induced renal damage.

Accumulating evidence indicates that KIM-1 — a transmembrane type-1 glycoprotein expressed at very low levels in healthy tubular epithelial cells —, is a sensitive biomarker for the early prediction of renal injury. Studies have shown that serum and urinary KIM-1 levels increase after acute ischemic injury and acute ischemic events in post-ischemic kidneys (Sabbisetti et al., 2014; Eirin et al., 2012). Mechanical compression of renal blood vessels and tubules due to excessive accumulation of fat in the RS may trigger hypoperfusion of the renal parenchyma and subsequent tubular injury. In support of this notion, authors found that sKIM-1 levels directly correlated with increments in RS adipose tissue, suggesting that tubular epithelial damage secondary to RS fat compression may be an important mechanism mediating obesity-induced renal damage.

Furthermore, the amount of RS adipose tissue directly correlated with serum levels of the adipokine FGF-21, a key mediator of fatty acid oxidation and lipid metabolism (Woo et al., 2013). Prospective studies have shown that serum FGF-21 is an independent predictor of kidney disease progression (Lee et al., 2015). In agreement, Krievina et al. found that FGF-21 inversely correlated with GFR, but directly correlated with the amount of RS adipose tissue, suggesting a link between RS fat accumulation and renal dysfunction.

The use of volumetric analysis and 3D reconstruction of various adipose tissue segments to assess RS fat content is an important strength to this study. This strategy offers important advantages over computed tomography or magnetic resonance single-scan measurements, which often lead to inaccurate results. In addition, authors measured RS adiposity in both kidneys, revealing asymmetrical RS adipose tissue accumulation, possibly due to anatomic and functional differences between the left and right kidney.

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Lastly, results of the one year follow-up study showed that accumulation of adipose tissue in the RS was associated with increased visceral adipose tissue volume, supporting their long term interaction. Contrarily, reductions in the amount of visceral adipose tissue did not affect RS adiposity, suggesting that weight loss may not correct RS fat accumulation. Additional prospective studies are warranted to determine whether dietary changes influence the amount RS fat and its association with renal dysfunction.

In summary, the results of this study suggest that RS adipose tissue effects should be assessed primarily on the left kidney, and imply that RS adipose tissue may be associated with an increased risk for tubular epithelial cell damage. Taken together, these observations shed light on the pathophysiological mechanisms underlying the contribution of RS adiposity to renal injury. Further studies are needed to establish a cause-effect relationship between RS adipose tissue and renal dysfunction.

Disclosures

The authors declare no competing interest.

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