Fat Chance for Hypertension and Chronic Kidney Disease

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Obesity is firmly associated with both hypertension and chronic kidney disease (CKD). Although these areas have been the subject of intense investigation over the last 2 decades, the mechanisms and best clinical indicators are not fully resolved. In the current issue, Foster et al provide intriguing evidence associating increased renal sinus fat (“fatty kidney”) specifically with increased prevalence of hypertension and CKD.

The prevalence of obesity continues to increase globally, as has occurred over the last few decades. Obesity has been definitively linked to hypertension and other cardiovascular diseases for many years. Numerous animal models and human studies have explored the mechanisms linking obesity to hypertension. Several factors have been consistently shown with obesity (Figure): increased sympathetic nervous system activity, increased renin-angiotensin-aldosterone system activity, and increased sodium reabsorption (and/or impaired pressure natriuresis) among other mechanisms.

A variety of adipocyte-derived factors, such as leptin, have also been shown to be involved. In addition, local or systemic inflammatory cascades, endothelial dysfunction, and reactive oxygen species likely have a role in the mechanistic links between obesity and hypertension.

The exact linkage between obesity and hypertension and other cardiovascular diseases, however, depends partly on the definitions and how body fat is measured. Central obesity (or abdominal obesity usually measured as waist circumference or waist:hip ratio) is more tightly associated with cardiovascular risk than simple body mass index, the more commonly used index. In fact, the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) used waist circumference rather than body mass index in defining metabolic syndrome. Metabolic syndrome is the constellation of some or all of abdominal obesity, elevated fasting glucose (indicating insulin resistance), hypertension, and dyslipidemia. Metabolic syndrome is a major risk factor for essentially all cardiovascular disorders. Although obesity and metabolic syndrome are highly correlated, there is not a 1-to-1 relationship. Abdominal fat consists of both visceral fat and subcutaneous fat. The visceral fat (consisting of omentum and mesentery fat) has some experimental and conceptual linkage to metabolic abnormalities because of portal drainage. For example, Okauchi et al reported that reduction of visceral fat was associated with a decrease in the number of metabolic risk factors, suggesting that metabolic syndrome may be a manifestation of (or caused by) visceral fat accumulation. Despite this, others have noted that subcutaneous fat has the larger mass and, hence, may have more impact.

The relationship between obesity (or metabolic syndrome) and CKD has only been established more recently but has now been confirmed in multiple studies. An increased prevalence of CKD occurs with each additional metabolic syndrome component. The mechanistic link with CKD has not been as well studied but is likely attributable to many of the same pathogenic mechanisms, with perhaps some additional factors, such as cellular lipotoxicity and fibrotic factors. Certainly, type 2 diabetes mellitus, the ultimate result of insulin resistance, accounts for close to 50% of end-stage renal disease.

In this complex background of linkage of adiposity, hypertension, and kidney disease, Foster et al, using a subset of the Framingham cohort (~2900 individuals), now specifically link high renal sinus fat with both hypertension and CKD. Although others have had similar suggestions, this report stands out as a large, community-based rigorous study. Foster et al quantified renal sinus fat and abdominal visceral adipose tissue with computed tomography, defining “fatty kidney” as greater than the 90th percentile of a nonobese healthy group. Fatty kidney so defined was present in almost one third of the subjects and was associated with a higher odds ratio of hypertension and chronic kidney disease even after adjusting for body mass index or abdominal visceral adipose tissue. The association with CKD was somewhat more questionable, in that the association was predominantly with a cystatin-based estimation of glomerular filtration rate. Cystatin-based estimates of glomerular filtration rate have proved valuable, but their use in practice is still undeveloped. The cystatin-based glomerular filtration rate could be affected by adipose tissue synthesis of cystatin, although the adjustment for body mass index would have been expected to adjust for this. The associations of fatty kidney with the longer standing, creatinine-based estimations of glomerular filtration rate were more tenuous in general. However, creatinine-based estimates also have potential issues.

The specificity and independence of the impact of renal sinus fat (after adjusting for visceral fat) were further suggested by the lack of association with more general metabolic derangements, such as diabetes mellitus or high glucose, increased triglycerides, or microalbuminuria. Although other studies have also shown that generalized obesity and visceral
Fat are strong predictors of renal sinus fat, the consequences may not be identical. The mechanism of the association between renal sinus fat and hypertension and/or kidney disease is speculative. But these authors, and other previous investigators, have noted the possible compression of renal vasculature, particularly renal veins. Increased renal venous pressure has clearly been shown in animal studies to cause sodium retention and hypertension. Of note, other investigators have documented toxicity of parenchymal or cellular lipids in the kidney.8

Certainly this new study represents a provocative finding both in terms of possible new mechanistic insight into some cases of hypertension and CKD but also conceivably clinical approaches in the future. Clinical use at the moment would be limited by the costly and inconvenient tools to assess renal fat; however, this might not be the case in the future, particularly under select conditions. A variety of future studies are needed to validate and expand these new findings. Longitudinal studies will be important to expand the current cross-sectional observations. Studies of other populations (eg, various ethnic groups and groups with more CKD) will be informative as well. New mechanistic studies should be done if the results are confirmed. Studies of particular determinants of renal sinus fat in contrast to more generalized location could be important. Our understanding of the interrelationships of obesity, hypertension, and CKD continues to grow, and this article marks an important new chapter. Once again, perhaps, location, location, location.

**Figure.** Speculative diagram of the relationships between aspects of obesity, hypertension (HTN), and chronic kidney disease (CKD). Generalized obesity, abdominal (or visceral) obesity, and fatty kidney largely overlap but may have distinct mechanistic links to HTN and CKD. SNS indicates sympathetic nervous system; RAAS, renin-angiotensin-aldosterone system; ROS, reactive oxygen species.

**References**


**Disclosures**

None.
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*Hypertension*. 2011;58:756-757; originally published online September 19, 2011; doi: 10.1161/HYPERTENSIONAHA.111.180414

*Hypertension* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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