JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
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PUBLISHED BY ELSEVIER INC.

VOL. 64, NO. 10, 2014
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2014.07.005

EDITORIAL COMMENT

Adiposity and Risk for Hypertension

Does Location Matter?*

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Obesity is a threat to global health, especially as a precursor and risk factor for fatal and nonfatal cardiovascular disease (1,2). The evidence for this conclusion can be presented in many ways, but perhaps the most dramatic expression is found in an extrapolation from the longitudinal Framingham study predicting that obese men have a shortening of lifespan of nearly 6 years, and women have a predicted shortening of 8 years compared with their nonobese neighbors (3). The suspected pathways linking obesity to eventual cardiovascular disease are diverse, and include insulin resistance, diabetes, hypertension, inflammation, and dyslipidemias. Among all those who are overweight, the presence of increased central obesity (elevated waist circumference or waist-hip ratio) conveys greater cardiovascular risk than body mass index (weight/height^2) (4). Visceral fat contributes a major fraction to central obesity and is located in the abdomen and intra-abdominal contents, in contrast to subcutaneous fat abundant in the buttocks and lower limbs. Rough clinical measurement of these components can be provided simply by the scale (weight) and tape measure (height, waist circumference) for routine clinical use, but modern imaging by magnetic resonance and x-ray densitometry have enhanced the anatomic compartmentalization of fat depots. Because localized fat deposits can now be defined by such methods, there is increased attention to the possible role of such sites as the heart, kidneys, and other organs (5).

In this issue of the *Journal*, Chandra et al. (6) provide new anatomic observations that may lead to increased focus on mechanisms whereby visceral obesity initiates hypertension or raises arterial pressure. In the Dallas Heart Study, the investigators characterized 903 obese, nonhypertensive participants, at baseline, by multiple biomarkers and by defining fat depots using magnetic resonance with proton-spectroscopic imaging and assessing lower body fat by dual energy x-ray absorptiometry.

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The techniques allowed them to identify visceral fat in the abdomen and retroperitoneal areas, as well as subcutaneous loci. During a follow-up interval of 7 years, 25% of the cohort became hypertensive (incident hypertension). It is not surprising that the initial statistical analysis found many differences between the hypertensive and nonhypertensive cohorts, as catalogued in Table 1 of the Chandra et al. study (6). Indeed, it is comforting that so many differences were consistent with earlier reports, (e.g., those who became hypertensive tended to have higher body mass indexes, more diabetes, and lower adiponectin levels). Body mass index was indeed correlated with incident hypertension. However, the size of the cohorts and the abundance of assessments allowed more extensive statistical analysis that exposed important distinct correlations.

After adjustment for various relevant correlates, Chandra et al. (6) found that visceral adiposity and, in particular, retroperitoneal fat were uniquely and selectively correlated with incident hypertension. These findings are consistent with the hypothesis that this pattern of adiposity is the result of overfeeding, such that subcutaneous fat depots have become filled, leading to overflow directed at abdominal and retroperitoneal sites. The new observation that retroperitoneal fat is the highest correlate with incident hypertension in this prospective study suggests that perirenal fat or perhaps periadrenal fat

*Editorials published in the *Journal of the American College of Cardiology* reflect the views of the authors and do not necessarily represent the views of *JACC* or the American College of Cardiology.

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might be the substrate for blood pressure-raising renal and/or adrenal mechanisms. Could a compressing effect of perirenal fat alter renal function via salt retention (7) or renin-mediated pathways to increase pressure over time, an adiposity-based Page kidney (8)? Could there be a link between retroperitoneal fat and adrenal incidentalomas? These "nonfunctional tumors" are associated with the metabolic syndrome (9). Is this association a reflection of subclinical adrenocortical hypertension leading to either primary aldosteronism or to Cushing's syndrome? The latter is clearly linked to diabetes and hypertension in its full-blown expression. Those obese individuals lacking the melanocortin 4 receptor tend to have less hypertension and reduced sympathetic activity (10), but do they also have less retroperitoneal fat? At present, it is unclear as to whether increased retroperitoneal fat is a cause or result of mechanisms that increase blood pressure associated with obesity.

The possible importance of retroperitoneal adiposity as a predictor of future hypertension implies the need for simple and practical methods to measure this particular fat depot in larger epidemiological surveys, especially when resources are limited. Further analysis of such a well-characterized prospective database provided by the Dallas Heart Study may unmask such methods. Although body mass index alone may be less accurate a predictor for incident hypertension than when it is combined with magnetic resonance imaging measurements of regional fat, it is reasonable health policy at this time to advocate that all obese individuals lose weight via diet and exercise until there is a compelling rationale for any alternate strategy related to regional fat excess.

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KEY WORDS magnetic resonance hypertension, obesity, retroperitoneum