Can Glucocorticoid Homeostasis Explain the Antiatherogenic Effect of Peripheral Adiposity?

To the Editor:

Tankó et al observed that peripheral adiposity in elderly women may be associated with a relatively reduced risk of insulin resistance, dyslipidemia, and vascular calcification. They suggested that this benefit reflects an antiatherogenic effect of peripheral fat. However, we believe their findings support the concept that subtly increased glucocorticoid activity may exert dysmetabolic and atherogenic effects. It is well known, for example, that supraphysiologic levels of glucocorticoids, as seen in Cushing syndrome, increase central adiposity at the expense of peripheral adiposity and muscle mass. In recent years, there has been increasing evidence that connects physiologically elevated endogenous glucocorticoid activity with visceral obesity—a phenomenon that may be mediated at the central level via increased activity of the hypothalamic-pituitary-adrenal (HPA) axis and at the peripheral level via increased conversion of cortisone to cortisol by 11-β-hydroxysteroid-dehydrogenase type 1 in adipose tissue. Increased activity of neuroendocrine stress axes—including elevated hypothalamic-pituitary-adrenal axis tone—has been linked to the metabolic syndrome and may contribute to the clustering of low HDL cholesterol, high triglycerides, insulin resistance, hypertension, and visceral obesity. In addition, there is in vitro evidence that glucocorticoids may contribute to vascular calcification.

In sum, the association between peripheral adiposity and favorable vascular risk factor profiles observed by Tankó et al may not be due to direct atheroprotective effects of peripheral fat per se. It is plausible that this association reflects a variation in endogenous glucocorticoid tone between the different groups—high glucocorticoid tone associated with central fat distribution and low glucocorticoid tone associated with peripheral fat distribution. It would be interesting to know whether other features of increased glucocorticoid activity, such as osteoporosis and decreased muscle mass, were more prevalent in those women with a more central fat distribution.

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