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Impact of Abdominal Adiposity on Cardiovascular Disease Predictors: What Is the Missing Link?

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The study by Majane *et al.* in this issue of the Journal[1] highlights the modifying role of age, in women only, on the independent deleterious effect of central adiposity on pulse wave velocity (PWV). In this sample of 508 randomly selected black South African subjects, older women had a 0.69 m/s increase in PWV, compared to a 0.16 m/s decrease in younger women, for a one s.d. increase in waist circumference (~13 cm). In the same vein, a one s.d. increase in waist-to-hip ratio (0.096 in older women and 0.076 in younger women) equated to a 0.58 m/s increase compared to a 0.16 m/s decrease in PWV in older vs. younger women, respectively. No association was observed between adiposity markers and augmentation index or aortic-brachial wave amplification. The authors postulate that the mediating effect of age on the adiposity–PWV association is likely to explain, at least in part, the negative findings of previous studies of predominantly younger and middle-aged subjects, which have been unable to demonstrate robust and independent relationships between adiposity markers and PWV. In addition, they argue that the inclusion of a large number of overweight and obese subjects in their study allowed detection of the age–adiposity interaction affecting PWV, which may not have been apparent in previous studies of predominantly leaner subjects, particularly if only BMI was measured. This may be the case, although we previously found a similar correlation between waist circumference and aortic PWV in 1,014 healthy subjects recruited from the SUVIMAX cohort, despite only 9% of the cohort being obese.[2] Although a high prevalence of obesity in the study by Majane *et al.* may strengthen the association with PWV, it is not likely to fully explain such discrepancy between studies because the links between PWV and body weight appears early in vascular development.[3]

The pathopysiological mechanisms linking abdominal adiposity to arterial stiffening, particularly in older subjects, remain under debate. It is possible that this association is partly mediated by insulin resistance. Visceral fat is a labile fat depot compared to subcutaneous fat, with lipolysis being less suppressed by insulin. Fatty acids impair large artery function directly via inhibition of endothelial nitric oxide production and impaired endothelial-dependent flow dilatation. Increased secretion of pro-inflammatory cytokines, such as tumor necrosis factor-α and leptin, and decreased production of anti-inflammatory adipokines such as adiponectin, are also likely to link abdominal fat and arterial stiffness. Finally, sympathetic neural activation resulting in higher vasomotor tone may also contribute. Indeed, hypertensive subjects and those with a high BMI, waist circumference, or the metabolic syndrome have been shown to exhibit increased pulse pressure amplification and increased heart rate.[4]

The study by Majane *et al.*[1] has confirmed the need for homogeneous and well-phenotyped populations to investigate the independent and complex relationship relating adiposity to intermediate cardiovascular markers. Further studies are required to elucidate additional factors linking adiposity *per se* to cardiovascular disease risk. Ideally, this should be undertaken using direct measures of total body and central abdominal fat to allow partitioning of each fat depot.[5] Capillary density will be also important to consider.

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