

One pitfall of reporting response is the phenomenon of “regression to the mean.” If enrollment requires a measurement below a certain threshold, using a test with an element of variability, such as LVEF, a measurement taken on 1 particular day might be lower than the patients’ true average value. When the test is repeated (after the intervention), the measurement is likely to have risen closer to the patients’ true average. This may give the false impression of a therapeutic improvement. Unless there is a control group for comparison, a reader may be misled into thinking that an intervention is effective. Describing an intervention as “effective” should be reserved for the findings of randomized controlled trials where there is a significant difference between the intervention and control groups.

The terms “outcome,” “response,” and “effect” are sometimes used interchangeably in imaging research. We suggest simple definitions to facilitate clear communication and avoid misinterpretation of findings and even of study design.

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## Qualitative Characterization of Adipose Tissue by MDCT

We read with great interest the paper by Rosenquist et al. (1) published recently in *JACC*. The analysis performed on a large cohort drawn from the Framingham Heart Study implies that lower multidetector computed tomography (MDCT) attenuation of subcutaneous adipose tissue and visceral adipose tissue is associated with an adverse cardiometabolic risk profile. We would like to reflect on 2 aspects of the published data.

First, although imaging of adipose tissue by MDCT offers relatively high resolution and reproducibility and has increasingly been used as a research tool, the methodology of computed tomography fat volume calculations has never been validated. Measurements are based on an arbitrary attenuation range (Hounsfield units), which is not set uniformly across the literature. Such attenuation-based identification may lead to the parts of adipose tissue with the lowest and highest attenuation being left unaccounted for. Furthermore, attenuation relies substantially on computed tomography scan parameters, especially tube voltage (kV), and also on patients’ characteristics. Tube voltage is often set differently for lean and obese patients. All of these factors may lead to a systematic bias in interpretation of a study such as that by Rosenquist et al. (1). Scan parameters applied in the reported cohort were not mentioned in the paper.

Second, we know from basic research studies that adipose tissue may display either an unfavorable or a favorable metabolic profile (endocrine and paracrine) depending on its location and metabolic status (2). As an example, epicardial adipose tissue in patients with coronary artery disease as opposed to patients without this disease showed intense leukocyte infiltration, thickened interlobular septa, and increased neovascularization (3). All of these elements are more radiodense than lipid-laden adipocytes and thus may lead to higher, rather than lower, MDCT attenuation of adipose tissue with a proinflammatory and proatherosclerotic metabolic profile. Results of our clinical study corroborate this hypothesis (4). Furthermore, as noted by Rosenquist et al. (1), lower attenuation of subcutaneous adipose tissue and visceral adipose tissue was correlated with fat volume because larger, lipid-laden adipocytes are less attenuating. In such circumstances, in a retrospective, cross-sectional study, it may be difficult to distinguish the effects of fat volume from those of its attenuation. Thus, it would be interesting to see how the attenuation correlated with cardiometabolic risk factors within subgroups with similar fat volumes.

To summarize, the study by Rosenquist et al. (1) adds significantly to the growing body of evidence on the research and clinical role of MDCT-derived characterization of adipose tissue. However, further research efforts to eliminate the aforementioned limitations are warranted. Longitudinal designs, histopathology references, methodological improvements, standardization of MDCT fat measurements, and prospective methods of accounting for the established confounding factors in adipose tissue attenuation and volume measurements should be clarified to further develop this new, fascinating area of research.

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## Myocardial Extracellular Volume Measurement by Cardiac Magnetic Resonance

Measuring myocardial extracellular volume (ECV) with cardiovascular magnetic resonance is achieving increasing importance because it allows quantification of diffuse fibrosis not detectable with conventional late gadolinium enhancement techniques. However, the *conditio sine qua*