COMMENTS AND RESPONSES

Pericardial Adipose Tissue, Atherosclerosis, and Cardiovascular Disease Risk Factors: The Jackson Heart Study

Response to Iacobellis and Malavazos

We acknowledge the comment made by Iacobellis and Malavazos (1) and appreciate the opportunity to address it further while clarifying some points. Anatomically, pericardial adipose tissue (PAT) is largely brown adipose tissue and is divided into two layers: epicardial and paracardial fat layers (2,3). In general, PAT is defined as epicardial plus paracardial adipose tissue (2–4). Likewise, using computed tomography or magnetic resonance imaging to provide a detailed anatomic display of the entire pericardium, the volumetric PATs were defined as any adipose tissue located in the pericardial sac (4). Thus, the terminology "pericardial" fat used in our study (5) is consistent with the current anatomical usage, which includes epicardial and paracardial adipose tissues.

We agree that there are numerous established differences between adipose tissue located in the epicardial space and the paracardial space (6). However, identifying the pericardium to distinguish true epicardial from paracardial adipose tissue based on the biology and the anatomic spaces cannot be visualized by all imaging modalities, including echocardiography (2). Current cardiac magnetic resonance imaging and computed tomography technology can differentiate the epicardial space from the paracardial space, but this task becomes increasingly difficult in lean individuals who have limited PATs. Furthermore, the results from the Multi-Ethnic Study of Atherosclerosis (MESA) have indicated that epicardial adipose tissue highly correlated with the combined measures of epicardial and paracardial adipose tissue ($r = 0.92$, $P < 0.0001$) and consequently has been utilized in the Jackson Heart Study. More importantly, emerging data have indicated that both epicardial adipose tissue and paracardial adipose tissue (or mediastinal fat) are equally metabolically active. Recent studies have demonstrated that uncoupling protein one (UCP-1) and brown adipocyte differentiation transcription factors PR-domain-missing16 (PRDM16) are significantly elevated in adipose tissue located in the pericardium as compared with subcutaneous fat (7). The adipose tissues in this location are also found to be a source of several inflammatory chemokines. Thus, the combined measures of epicardial and paracardial adipose tissues in our study have maximally minimized the error and misclassification.

In summary, the PAT by definition in our study is the sum of epicardial and paracardial adipose tissues because both of them are a source of several inflammatory chemokines and are metabolically equally active. The results from our study highlight the importance of PAT in the relationships to the cardiometabolic risk and the local vasculature, which are consistent with the findings from the study among participants of European ancestry (4). Careful examination of epicardial and paracardial adipose tissues is required to determine their impact on the cardiometabolic risk factors and the coronary vasculature in the future.

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