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COMMENT ON PATEL ET AL.

ACE2 Deficiency Worsens Epicardial Adipose Tissue Inflammation and Cardiac Dysfunction in Response to Diet-Induced Obesity. Diabetes 2016;65:85–95

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We read with interest, but concern, the recently published article by Patel et al. (1) in *Diabetes*, which focused on potential links between angiotensin-converting enzyme 2 (ACE2) deficiency, epicardial adipose tissue (EAT) inflammation, and cardiac dysfunction in a high-fat diet mouse model.

The human heart is coated by fat whose function is becoming a hot topic in cardiovascular research. Indeed, EAT, i.e., the fat depot beneath the visceral pericardium and in direct contact with the epicardium, is a source of free fatty acids, adipokines, and inflammatory cytokines (2). EAT is thus believed to directly interact with cardiomyocytes in both physiology and pathology through paracrine signaling. To support this paradigm, recent epidemiological studies have linked EAT volume with cardiovascular disease, such as atrial fibrillation and coronary atherosclerosis (2).

Very few studies have reported on EAT in animal models as epicardial fat is known to be virtually absent in rodents usually used for most studies, i.e., mice and rats (2,3).

This limitation of rodent models has been recently "confirmed" by Böhm et al. (4) and Yamaguchi et al. (5). The latter reported that no epicardial fat could be observed in wild-type C57BL/6 mice. EAT developed at the atrioventricular groove when peroxisome proliferator–activated receptor-γ expression was forced. However, only minute amounts of fat, as small as 0.1 mm^3, were found (5).

Surprisingly, Patel et al. (1) reported amounts of EAT as high as 10 mg (more than 10 mm^3) in the same wild-type C57BL/6 mouse, in discrepancy with previous reports. One should be reminded that the normal left ventricle weighs no more than 100 mg in the mouse. Although the fat explored has been described to be dissected from the heart after removal of the pericardium, this large discrepancy raises concern regarding the origin of the studied adipose tissue, i.e., mediastinal or pericardial versus epicardial fat.

As very little or no EAT is seen in mice, we would therefore draw attention to the following points: *1*) any conclusion regarding interactions between the so-called EAT and cardiomyocytes in mice should be viewed with caution, *2*) attributing any pathophysiologic role of the so-called EAT to cardiac dysfunction from studies in these animals seems hazardous, and *3*) mice are a poor model to understand the role of EAT in human disease.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

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