Weight of Pericardial Fat on Coronaropathy

Karine Clément, Arnaud Basdevant, Anne Dutour

The regional distribution of adipose tissue (AT) is a major determinant of metabolic and cardiovascular diseases. The mass of fat in the visceral area associates independently of obesity with the development and progression of cardiovascular diseases in a series of clinical and epidemiological studies. This led to the concept of a pathophysiological link between abdominal obesity and metabolic syndrome. More recently, fat depots localized around the heart, highly variable among individuals, were proposed to contribute to the pathogenesis of coronaryopathy independently of other visceral depots (ie, in the omental and mesenteric area). The study by Greif et al in this issue of Arteriosclerosis, Thrombosis, and Vascular Biology highlights the association between pericardial adipose tissue (PAT) and the number of atherosclerotic plaques evaluated concomitantly by Dual source CT scan. This measurement was qualitatively interpretable in 264 consecutive patients with a large range of age, a normal or moderately increased body mass index (BMI), and no a priori coronary disease. An estimated volume of pericardial fat more than 300 cm³ provided an incremental value for the presence of coronary atherosclerosis (odds ratio 4.1) independently of well known risk factors (hyperglycemia or diabetes, hypercholesterolemia, hypertension, and smoking). Ninety-five percent of patients with PAT volume >300 cm³ had one or more atherosclerotic plaques by ROC estimation. In univariate statistical analysis, PAT volume was correlated with adipose tissue-derived inflammatory biomarkers like TNFα and adiponectin. Intriguingly the amount of PAT was not related to the severity of vascular alteration; ie, the mass of PAT was similar in subjects with noncalcified and in those with advanced calcified plaques. Based on the finding that young subjects with early stage plaques revealed a significant increase in PAT volume, it is suggested that PAT augmentation could precede the formation of plaque calcification and mature atherosclerotic plaque. The authors propose that PAT volume could be used for risk stratification in the absence of coronary calcium. Though practical constraints (cost and radiation exposure) limit the routine use of CT scan to estimate individual cardiovascular risk at the population level, this study contributes to the fascinating discussion regarding the potentially causal role of fat abundance around the heart in coronary atherosclerosis. It also provides new insight into the appropriate quantification and phenotyping of this depot as a new estimate of visceral fat. It is worthwhile mentioning that the measured “pericardial fat” is composed of epicardial fat (the epicardial adipose tissue (EAT) depot immediately adjacent to the heart wall, see Figure) and of the paracardial fat located on the external surface of the pericardium (ie, Mediastinal fat). The authors estimated in a subset of 120 subjects that both epicardial and pericardial fat volume were strongly correlated and related equally to the number of atherosclerotic plaques. This observation is interesting as far as EAT and paracardial fat do not share the same embryological origin (and vascularization) and as the pathophysiological role of paracardial fat is unknown. Furthermore, EAT lacks fascia and shares the same vascularization as the myocardium (ie, coronary arteries). EAT-derived bioactive molecules such as inflammatory, immune, and oxidative stress mediators and local fatty acids are pathophysiological candidates for the development of atherogenesis via diffusion in interstitial fluid across the adventitia and the arterial media, or transport via the vasa vasorum to cells of the atherosclerotic plaque. In vitro studies have shown that paracrine dialogs between human adipocytes and inflammatory cells present in adipose tissue (ie, macrophage, lymphocytes, and others) promote an increased synthesis of numerous biomolecules, leading to a low-grade inflammatory microenvironment. These conditions most likely promote plaque formation. The precise characterization of EAT-produced molecules, their cell origin, and their impact on epicardial adipocytes and myocardial biology remain to be identified. Gene expression studies have shown that EAT in obese patients who are candidates for coronary artery bypass graft appears more inflammatory than subcutaneous fat located in the legs. It was suggested that the inflammation state of EAT could lead to aggravation of vascular inflammation, plaque instability, and neovascularization. EAT could also exert a protective effect through the well-known buffering property of adipose tissue for toxic fatty acids, through the local secretion of adiponectin and adrenomedullin, or by providing additional energy to increased ventricular mass. This study also raises new questions concerning the contribution of paracardial fat to these metabolic and inflammatory alterations and of their consequences for coronary atherosclerosis. Although no clear link between PAT and the severity of coronaryopathy (ie, presence of calcified and uncalcified plaques) was established in this imaging study, the need for understanding both the physiological and pathophysiological links between this tissue and myocardial homeostatic function in subjects without and with coronaryopathy is essential.
Because this putative link might be modified in the complex stages of evolution of coronaropathy in individuals with various risk factors (incl. insulin resistance state), pathologies, and treatments, both the exploration of pericardial fat in different human conditions and the use of animal models prone to EAT expansion (ie, guinea pigs, rabbits, primates) are needed. Finally, the increased volume of EAT and its association with the low-grade inflammatory process could reflect a contribution to a more global phenomenon of visceral fat expansion as suggested by positive associations found between EAT measured by ultrasonography, surrogate markers of intraabdominal fat, or anthropometric measurement performed in autopsy studies (reviewed in References 1, 2, 3). Visceral fat, now well recognized as a risk depot for cardiovascular disease, is usually estimated in clinical studies by the measure of waist circumference, a parameter not evaluated in this study. The report of Greif et al illustrates the need to investigate the additional benefit of precisely quantifying pericardial fat per se (rather than detecting it as a morphological sign of coronary alteration) as a valuable and independent coronaropathy risk factor or as a marker of visceral abdominal fat, which is known to be inflamed in metabolic disease.

Acknowledgments
The authors thank the ADAPT European Community’s 7th Framework Programme (FP7-HEALTH-2007-A), promoting the research on the adverse role of adipose tissues on inflammation related diseases (http://www.adapt-eu.net/) as well as Prof Juergen Eckel and Dr Henrike Sell for helpful suggestions.

Disclosures
None.

Figure. Schematic role of EAT in the alteration of myocardial homeostasis. EAT volume can augment and pericardial fat composed of both EAT and paracardial fat with a volume >300 cm³ strongly increased the risk of atherosclerotic plaques. Here only EAT is shown. Multiple adipose-derived molecules can contribute to the alteration of myocardial homeostasis. Noteworthy, the altered capacity of fat storage in subcutaneous adipose tissues is a factor favoring visceral fat depots such as EAT (visc) as well as ectopic fat accumulation. sc indicates subcutaneous.

References
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Arterioscler Thromb Vasc Biol. 2009;29:615-616
doi: 10.1161/ATVBAHA.108.182907
Arteriosclerosis, Thrombosis, and Vascular Biology is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 1079-5642. Online ISSN: 1524-4636

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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