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The Association of Epicardial Fat Thickness to Cardiovascular Clinical Outcomes

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INTRODUCTION

Epicardial fat is a visceral fat deposit which is located between the heart and the pericardium sharing many of the patho-physiological properties of other visceral fat deposits. There is recognition of three functional types of adipose tissue. The first type, the white adipose tissue consists of large unilocular adipocytes whose primary function is to store energy in the form of triglyceride. The second type, the brown adipose tissue which contains multilocular adipocytes with large numbers of mitochondria, this is most commonly found in young mammals and rodents. Its primary function is to generate heat via uncoupled oxidative phosphorylation. Third, the beige adipose tissue is form of brown adipocytes that arises within the white adipose depots and also has thermogenic capacity [1-7]. It is important to differentiate between the adipose tissue located on the outer surface of the fibrous pericardium (paracardial fat) from the one in the inner surface of the visceral pericardium (epicardial fat) which is in direct contact with the myocardium and the epicardial vessels, since they differ in their biochemical, molecular and vascular nutrition properties. The paracardial fat is nourished by the pericardiophrenic artery, a branch of the internal thoracic artery, while the epicardial fat is nourished by the coronary arteries [8-11]. The epicardial fat is more prominent in the atrioventricular and interventricular grooves and right ventricular lateral wall. Adipocyte infiltration into the myocardium wall as well as triglyceride infiltration into myocytes may also occur. The paracardial fat has been also called intrathoracic, mediastinal or pericardial. In addition, some other groups treat these different fat deposits as a single compartment, calling it pericardial fat [12-16]. Since several studies have observed a moderate association between EFT and cardiovascular clinical outcomes, it is important to analyze this relationship at the light of medicine based evidence.

Epicardial fat thickness (EFT) can be measured by different imaging modalities. Magnetic resonance imaging (MRI) is considered the gold standard for the assessment of total body fat and reference modality for the analysis of ventricular volumes and mass, thus making it a natural choice for the detection and quantification of EFT [17-19]. For purposes of cardiovascular risk stratification, measurement of EFT using echocardiography has generally been the study of choice, due to its lesser cost, ease of use, and absence of radiation. By echocardiography, measurements of the right ventricular free wall from both parasternal longitudinal and transverse parasternal views should be performed using the mean of three consecutive beats. These echocardiographic measurements show good correlation with the values found on MRI ($r = 0.91$, $p = 0.001$) [19]. There are some controversial issues in the EFT measurements by echocardiography. For example, there are some inconsistencies in the site of measurement due to spatial variations of the echocardiographic window, especially along the great vessels and the right ventricle. In addition, it is uncertain yet which moment of the cardiac cycle is the most suitable for measuring EFT by echocardiography. Some recommend the measurement during systole to prevent possible deformation by compression of the epicardial fat during diastole (8). On the other hand, other researchers prefer measurements in diastole to coincide with measurements of other imaging modalities like CT scans and MRI [19-21].

Although there are some studies that suggested higher cutoffs, measurements greater than 5 mm should represent a relevant cutoff to define increased EFT in low-risk population. The mean value described for EFT in systole was 6.8 mm (1.1 to 22.6 mm) [22]. In obese patients, the mean value of EFT was 9.5 mm (7.0 to 20.0 mm) for men, and 7.5 mm (6.0 - 5.0 mm) for women [23]. When measurements were performed in diastole in patients who underwent coronary angiography, the mean value was 6.4 mm (1.1 to 16.6 mm) [24]. It was also demonstrated in asymptomatic patients an EFT with a mean value of 4.7 ± 1.5 mm [25]. According to current knowledge, an EFT greater than 5 mm, or an epicardial fat volume greater than 125 mL or 68 mL/m² may be considered abnormal.

Several studies have observed a moderate association be-

tween EFT and clinical outcomes. In a case-control study of incident cases during a four-year follow-up, Cheng et al. [26] compared 58 patients with major adverse cardiac events with 174 controls free of events. The patients were matched by sex and a propensity risk score that included age, risk factors and coronary calcium score. The researchers demonstrated a higher risk of events (OR = 1.74, 95% confidence interval [95% CI]: 1.03-2.95) with a two-fold increase in epicardial fat volume. In the MESA (Multi-Ethnic Study of Atherosclerosis) cohort, Ding et al. investigated a random sample of 998 participants and the 147 individuals who developed coronary events [16]. Epicardial fat was associated with coronary artery disease (relative risk for increase of one standard deviation = 1.26, 95% CI: 1.01-1.59) even after adjustment for cardiovascular risk factors [16]. Moreover, associations between EFT and coronary artery calcification were found both in the Framingham and in the MESA studies [15, 27]. It is well known that coronary artery calcification has been used as a marker of subclinical atherosclerosis in representative population samples. Additionally, it is speculated that the increase in EFT and fatty infiltration of the myocardium may cause other deleterious cardiovascular effects, such as interfering with diastolic relaxation, affecting the cardiac conduction system and predisposing to atrial fibrillation. EFT is inversely associated with ejection fraction and left ventricular mass [28-30].

The EFT could add significant incremental values beyond the conventional clinical and echocardiography parameters in prediction of adverse cardiovascular outcomes. EFT has been proposed to influence the development of coronary atherosclerosis owing to its endocrine and paracrine activity by secreting anti-inflammatory and pro-inflammatory cytokines and chemokines [31-35]. In patients with documented coronary artery disease, Jeong et al. demonstrated that EFT was correlated significantly with its severity of atherosclerosis [36]. Several studies also showed that age and body mass index were associated significantly with EFT. Increased EFT is strongly associated with diabetes mellitus, cardiovascular disease, visceral obesity, subclinical atherosclerosis at multiple locations, and the metabolic syndrome [34-39]. EFT is also increased in subjects with atrial fibrillation and correlates with atrial fibrillation severity and its recurrence after catheter ablation [40-42]. In non-AF patients, increased EFT is shown to be positively associated with the severity of coronary artery disease and left ventricular diastolic dysfunction and is a useful parameter in predicting adverse cardiovascular events [43-46]. An association between EFT and incident myocardial infarction and cardiovascular risk factors were observed in the general population. In the cross-section study by Akil et al. the EFT in patients diagnosed with ischemic stroke was found to be higher than those in healthy controls [35]. Therefore, EFT could provide incremental value for cardiovascular outcome prediction over traditional clinical and echocardiographic parameters.

REFERENCES

1. Kremen J, Dolinkova M, Krajickova J, Blaha J, et al. (2006). Increased subcutaneous and epicardial adipose tissue production of proinflammatory cytokines in cardiac surgery patients: possible role in postoperative insulin resistance. J Clin Endocrinol Metab. 91(11), 4620-4627.

2. Kiefer FW, Cohen P and Plutzky J. (2012). Fifty shades of brown: perivascular fat, thermogenesis, and atherosclerosis. Circulation. 126(9), 1012-1015.

3. Petrovic N, Walden TB, Shabalina IG, Timmons JA, et al. (2010). Chronic peroxisome proliferator-activated receptor gamma (PPARgamma) activation of epididymally derived white adipocyte cultures reveals a population of thermogenically competent, UCP1-containing adipocytes molecularly distinct from classic brown adipocytes. J Biol Chem. 285(10), 7153-7164.

4. Cypess AM, Lehman S, Williams G, Tal I, et al. (2009). Identification and importance of brown adipose tissue in adult humans. N Engl J Med. 360(15), 1509-1517.

5. Vanhommerig JW, Smulders NM, Drossaerts JM, Kemerink GJ, et al. (2009). Cold-activated brown adipose tissue in healthy men. N Engl J Med. 360(15), 1500-1508.

6. Nedergaard J and Cannon B. (2010). The changed metabolic world with human brown adipose tissue: therapeutic visions. Cell Metab. 11(40), 268-272.

7. Tam CS, Lecoultre V and Ravussin E. (2012). Brown adipose tissue: mechanisms and potential therapeutic targets. Circulation. 125(22), 2782-2791.

8. Iacobellis G and Willens HJ. (2009). Echocardiographic epicardial fat: a review of research and clinical applications. J Am Soc Echocardiogr. 22(12), 1311-1319.

9. Verhagen SN and Visseren FL. (2011). Perivascular adipose tissue as a cause of atherosclerosis. Atherosclerosis. 214(1), 3-10.

10. Wang ZJ, Reddy GP, Gotway MB, Yeh BM, et al. (2003). CT and MR imaging of pericardial disease. Radiographics. 23, S167-S180.

11. Fox CS, Gona P, Hoffmann U, Porter SA, et al. (2009). Pericardial fat, intrathoracic fat, and measures of left ventricular structure and function: the Framingham Heart Study. Circulation 119(12), 1586-1591.

12. Mahabadi AA, Massaro JM, Rosito GA, Levy D, et al. (2009). Association of pericardial fat, intrathoracic fat, and visceral abdominal fat with cardiovascular disease burden: the Framingham Heart Study. Eur Heart J. 30(7), 850-856.

13. Nelson AJ, Worthley MI, Psaltis PJ, Carbone A, et al. (2009). Validation of cardiovascular magnetic resonance assessment of pericardial adipose tissue volume. J Cardiovasc Magn Reson. 11, 15.

14. Yun KH, Rhee SJ, Yoo NJ, Oh SK, et al. (2009). Relationship between the echocardiographic epicardial adipose tissue

thickness and serum adiponectin in patients with angina. J Cardiovasc Ultrasound. 17(4), 121-126.

15. Rosito GA, Massaro JM, Hoffmann U, Ruberg FL, et al. (2008). Pericardial fat, visceral abdominal fat, cardiovascular disease risk factors,and vascular calcification in community-based sample: the Framingham Study. Circulation Heart. 117(5), 605-613.

16. Ding J, Hsu FC, Harris TB, Liu Y, et al. (2009). The association of pericardial fat with incident coronary heart disease: the Multi-Ethnic Study of Atherosclerosis (MESA). Am J Clin Nutr. 90(3), 499-504.

17. Ross R, Shaw KD, Martel Y, de Guise J, et al. (1993). Adipose tissue distribution measured by magnetic resonance imaging in obese women. Am J Clin Nutr. 57(4), 470-475.

18. Machann J, Thamer C, Schnoedt B, Haap M, et al. (2005). Standardized assessment of whole body adipose tissue topography by MRI. J Magn Reson Imaging. 21(4), 455-462.

19. Iacobellis G, Ribaudo MC, Assael F, Vecci E, et al. (2003). Echocardiographic epicardial adipose tissue is related to anthropometric and clinical parameters of metabolic syndrome: a new indicator of cardiovascular risk. J Clin Endocrinol Metab. 88(11), 5163-5168.

20. Natale F, Tedesco MA, Mocerino R, de Simone V, et al. (2009). Visceral adiposity and arterial stiffness: echocardiographic epicardial fat thickness reflects, better than waist circumference, carotid arterial stiffness in a large population of hypertensives. Eur J Echocardiogr. 10(4), 549-555.

21. Mookadam F, Goel R, Alharthi MS, Jiamsripong P, et al. (2010). Epicardial fat and its association with cardiovascular risk: a cross-sectional observational study. Heart Views. 11(3), 103-108.

22. Iacobellis G, Willens HJ, Barbaro G and Sharma AM. (2008). Threshold values of high-risk echocardiographic epicardial fat thickness. Obesity (Silver Spring). 16(4), 887-892.

23. Iacobellis G, Singh N, Wharton S and Sharma AM. (2008). Substantial changes in epicardial fat thickness after weight loss in severely obese subjects. Obesity (Silver Spring). 16(7), 1693-1697.

24. Jeong J, Jeong MH, Yun KH, Oh SK, et al. (2007). Echocardiographic epicardial fat thickness and coronary artery disease. Circ J. 71(4), 536-539.

25. Nelson MR, Mookadam F, Thota V, Emani U, et al. (2011). Epicardial fat: an additional measurement for subclinical atherosclerosis and cardiovascular risk stratification? J Am Soc Echocardiogr. 24(3), 339-345.

26. Cheng VY, Dey D, Tamarappoo B, Nakazato R, et al. (2010). Pericardial fat burden on ECG-gated noncontrast CT in asymptomatic patients who subsequently experience adverse cardiovascular events. JACC Cardiovasc Imaging. 3(4), 352-360.

27. Ding J, Kritchevsky SB, Hsu FC, Harris TB, et al. (2008). Association between non-subcutaneous adiposity and calcified coronary plaque: a sub-study of the Multi-Ethnic Study of Atherosclerosis. Am J Clin Nutr. 88(3), 645-650.

28. Thanassoulis G, Massaro JM, O'Donnell CJ, Hoffmann U, et al. (2010). Pericardial fat is associated with prevalent atrial fibrillation: the Framingham Heart Study. Circ Arrhythm Electrophysiol. 3(4), 345-350.

29. Wong CX, Abed HS, Molaee P, Nelson AJ, et al. (2011). Pericardial fat is associated with atrial fibrillation severity and ablation outcome. J Am Coll Cardiol. 57(17), 1745-1751.

30. Liu J, Fox CS, Hickson DA, May WL, et al. (2011). Pericardial fat and echocardiographic measures of cardiac abnormalities: the Jackson Heart Study. Diabetes Care. 34(2), 341-346.

31. Mazurek T, Zhang L, Mannion JD, Zalewski A, et al. (2003). Human epicardial adipose tissue is a source of inflammatory mediators. Circulation. 108(20), 2460-2466.

32. Laine P, Kaartinen M, Penttila A, Panula P, et al. (1999). Association between myocardial infarction and the mast cells in the adventitia of the infarct-related coronary artery. Circulation. 99(3), 361-369.

33. Hirata Y, Tabata M, Kurobe H, Motoki T, et al. (2011). Coronary atherosclerosis is associated with macrophage polarization in epicardial adipose tissue. J Am Coll Cardiol. 58(3), 248-255.

34. Park JS, Ahn SG, Hwang JW, Lim HS, et al. (2010). Impact of body mass index on the relationship of epicardial adipose tissue to metabolic syndrome and coronary artery disease in an Asian population. Cardiovasc Diabetol. 9, 29.

35. Akil E, Akil MA, Varol S, Özdemir HH, et al. (2014). Echocardiographic epicardial fat thickness and neutrophil to lymphocyte ratio are novel inflammatory predictors of cerebral ischemic stroke. J Stroke Cerebrovasc Dis. 23(9), 2328-2334.

36. Jeong JW, Jeong MH, Yun KH, Oh SK, et al. (2007). Echocardiographic epicardial fat thickness and coronary artery disease. Circ J. 71(4), 536-539.

37. Karastergiou K and Fried SK. (2013). Multiple adipose depots increase cardiovascular risk via local and systemic effects. Curr Atheroscler Rep. 15(10), 361.

38. Natale F, Tedesco MA, Mocerino R, De Simone V, et al. (2009). Visceral adiposity and arterial stiffness: echocardiographic epicardial fat thickness reflects, better than waist circumference, carotid arterial stiffness in a large population of hypertensives. Eur J Echocardiogr. 10(4), 549-555.

39. Iacobellis G, Ribaudo MC, Assael F, Vecci E, et al. (2003). Echocardiographic epicardial adipose tissue is related to anthropometric and clinical parameters of metabolic syndrome: a new indicator of cardiovascular risk. J Clin Endocrinol Metab. 88(11), 5163-5168.

40. Bos D, Shahzad R, Walsum TV, Hofman A, et al. (2015). Epicardial fat volume is related to atherosclerotic calcification in multiple vessel beds. Eur Heart J Cardiovasc Imag. 16, 1264-1269.

41. Al Chekakie MO, Welles CC, Metoyer R, Ibrahim A, et al. (2010). Pericardial fat is independently associated with human atrial fibrillation. J Am Coll Cardiol. 56(10), 784-788.

42. Tsao HM, Hu WC, Wu MH, Tai CT, et al. (2011). Quantitative analysis of quantity and distribution of epicardial adipose tissue surrounding the left atrium in patients with atrial fibrillation and effect of recurrence after ablation. Am J Cardiol. 107(10), 1498-1503.

43. Chao TF, Hung CL, Tsao HM, Lin YJ, et al. (2013). Epicardial adipose tissue thickness and ablation outcome of atrial fibrillation. PLoS One. 8(9), e74926.

44. Park HE, Choi SY and Kim M. (2014). Association of epicardial fat with left ventricular diastolic function in subjects with metabolic syndrome: assessment using 2-dimensional echocardiography. BMC Cardiovasc Disord. 14, 3.

45. Mahabadi AA, Berg MH, Lehmann N, Kälsch H, et al. (2013). Association of epicardial fat with cardiovascular risk factors and incident myocardial infarction in the general population: the Heinz Nixdorf Recall Study. J Am Coll Cardiol. 61(13), 1388-1395.

46. Ulucan S, Kaya Z, Efe D, Keser A, et al. (2015). Epicardial fat tissue predicts increased long-term major adverse cardiac event in patients with moderate cardiovascular risk. Angiology. 66(7), 619-624.