Indian Heart Journal 72 (2020) 445–447

Contents lists available at ScienceDirect

Indian Heart Journal

journal homepage: www.elsevier.com/locate/ihj

Research Brief

Study of correlation between epicardial fat thickness and severity of coronary artery disease

Sunil Kumar Shambu [a, *], Nagaraj Desai [b], Nikhil Sundaresh [c], M. Suresh Babu [d], B. Madhu [e], Oliver Joel Gona [f]

[a] Head, Department of Cardiology, JSS Medical College and Hospital, JSS Academy of Higher Education and Research, SS Nagar, Mysore 15, India
[b] Department of Cardiology, JSS Medical College and Hospital, JSS Academy of Higher Education and Research, SS Nagar, Mysore 15, India
[c] Dept. of Medicine, AJ Institute of Medical Sciences, Mangalore, India
[d] JSS Medical College and Hospital, JSS Academy of Higher Education and Research, SS Nagar, Mysore, 15, India
[e] Department of Community Medicine, JSS Medical College and Hospital, JSS Academy of Higher Education and Research, SS Nagar, Mysore 15, India
[f] Department of Pharmacy Practice, JSS College of Pharmacy, JSS Academy of Higher Education and Research, SS Nagar, Mysore 15, India

ARTICLE INFO

Article history:
Received 31 March 2020
Accepted 7 July 2020
Available online 17 July 2020

Keywords:
Epicardial fat thickness
Echocardiography
Gensini score
Coronary artery disease

ABSTRACT

Epicardial fat thickness (EFT) reflects visceral adiposity and is associated with coronary artery disease (CAD). This study aimed to assess the correlation of echocardiographic EFT with the severity of CAD and to determine the EFT cut-off to predict CAD. EFT was measured in 503 patients undergoing coronary angiogram. Mean EFT was significantly higher in the CAD group than control group (5.55 ± 1.21 mm vs 3.25 ± 1.15 mm, $p < 0.0001$). EFT correlated with Gensini score ($r = 0.906$, $p < 0.001$). EFT cut-off ≥ 4.75 mm had 87% sensitivity and 63% specificity for prediction of significant CAD (AUC: 0.831, $p < 0.001$).

1. Introduction

Visceral fat, perhaps more than total fat is implicated in atherosclerosis.[1] Epicardial adipose tissue (EAT), a non-traditional visceral fat depot modulates coronary arteries through paracrine or vasocrine secretion of bioactive adipokines.[2] EAT thickness can be measured by transthoracic echocardiography, cardiac CT, and cardiac MRI methods. Studies have documented an association between echocardiographic EFT and CAD.[3–5] This study was designed to assess correlation of EFT with severity of CAD and to determine EFT cut-off to predict significant CAD in Indian population.

2. Materials and methods

This is a cross-sectional observational study conducted in the Cardiology department, JSS Hospital, Mysore. 587 patients underwent coronary angiogram from February 2017 to January 2019. 503 patients were eligible for the analysis. Patients less than 18 years of age, poor acoustic window, not willing to give consent, k/c/o CAD - thrombolysed in the past or had undergone revascularization and minimal CAD were excluded from the study. Informed consent was taken. Institutional ethical committee approval was taken.

Transthoracic echocardiography was done by using Phillips HD 11XE ultrasound machine. EFT was measured prior to coronary angiogram except in STEMI where it was measured within 24 hours. Echocardiographers measuring EFT were blinded from patients' clinical and angiographic data. Epicardial fat was measured perpendicularly on the free wall of the right ventricle at end-systole in parasternal short axis and parasternal long axis views in 3 cardiac cycles. The average value of 3 cardiac cycles was determined.[5]

Subjects were classified into control group (Normal coronaries) and CAD group (Significant coronary artery stenosis). Significant stenosis was defined as diameter stenosis of ≥50% in left main coronary artery and ≥70% in other major epicardial vessels. CAD

* Corresponding author. Head, Department of Cardiology, JSS Medical College and Hospital, JSS Academy of Higher Education and Research, SS Nagar, Mysore – 15, India.
E-mail addresses: sunil_cardio@yahoo.co.in (S.K. Shambu), desai_nagaraj@yahoo.co.in (N. Desai), dr.nikhilsundresh@gmail.com (N. Sundaresh), drmsureshbabu@yahoo.co.in (M.S. Babu), madhub@jssuni.edu.in (B. Madhu), gonaoj@gmail.com (O.J. Gona).

https://doi.org/10.1016/j.ihj.2020.07.014

group was classified into single, double and triple vessel disease (SVD, DVD & TVD). Gensini score was used for quantifying CAD severity.[6]

3. Statistical analysis

Descriptive and appropriate inferential statistics (parametric & non-parametric) were applied using SPSS (Version 25.0). ROC analysis and area under the curve (AUC) was calculated to derive EFT cut-off. Statistical significance was defined as $P < 0.05$.

4. Results

4.1. Demographics

Among 503 subjects, 18.3% (n = 92) had normal coronary arteries and 81.7% (n = 411) had significant CAD. 35.5% (n = 146) had SVD, 30.9% (n = 127) had DVD and 33.6% (n = 138) had TVD. Patient characteristics are depicted in Table 1. Acute coronary syndrome (ACS) was common indication for coronary angiogram [n = 386 (76.73%)].

4.2. Epicardial Fat Thickness (EFT) & severity of coronary artery disease (CAD)

The mean EFT was higher in the CAD group compared to the control group (5.5 ± 1.21 mm vs 3.25 ± 1.15 mm, $p < 0.0001$). There was a graded increase in EFT with increasing severity of CAD (Normal coronaries: 3.25 ± 1.15 mm, SVD: 4.71 ± 1.05 mm, DVD: 5.36 ± 1.14 mm, TVD: 6.6 ± 1.24 mm, $p < 0.001$). EFT had positive correlation with severity of coronary artery disease as assessed by Gensini score ($r = 0.906$, $p < 0.001$).

4.3. EFT and clinical variables

Age ($r = 0.259$, $p < 0.001$) and Waist circumference ($r = 0.413$, $p < 0.001$) had positive correlation with EFT. Men had higher mean EFT values when compared to women (5.05 ± 1.23 mm vs 4.38 ± 1.02 mm, $p < 0.001$). Patients with diabetes mellitus and hypertension had higher mean EFT values ($p < 0.05$). No significant correlation was found between EFT and BMI.

EFT cut-off ≥ 4.75 mm had a sensitivity of 87% and specificity of 63% (AUC: 0.831, $p < 0.001$) for predicting CAD. EFT cut-off ≥ 4.5 mm had a sensitivity of 98% and specificity of 44% (AUC: 0.307, $p = 0.04$) which was not statistically significant for predicting SVD. However, cut-off ≥ 5.2 mm for DVD and 6.2 mm for TVD prediction was statistically significant (AUC: 0.80 and 0.88 respectively, $p < 0.001$) Fig. 1.

Table 1
Patient characteristics.

Parameter	No CAD (n = 92)	CAD (n = 411)	p-Value
Age (years)	57.42 ± 13	61.7 ± 11.02	0.0012[a]
Body Mass Index (kg/m2)	23.61 ± 3.16	25.74 ± 3.37	<0.0001[a]
Males	62 (67.39%)	257 (62.53%)	0.38
Females	30 (32.6%)	154 (37.46%)	
Dyslipidaemia	10 (11)	78 (19)	0.06
Type 2 Diabetes Mellitus	33 (35.9)	221 (53.8)	0.0019[a]
Hypertension	33 (35.9)	201 (48.9)	0.02[a]
Smoking	29 (31.5)	179 (43.5)	0.03[a]
Alcohol	21 (22.8)	99 (24.08)	0.67
GENSINI Score	0	51.08 ± 29.07	<0.0001[a]
Systolic EFT (mm)	3.25 ± 1.15	5.55 ± 1.21	<0.0001[a]

[a] Statistical significance (p-value <0.05) has been obtained by comparing means using *t*-test and proportions by using chi-square test.

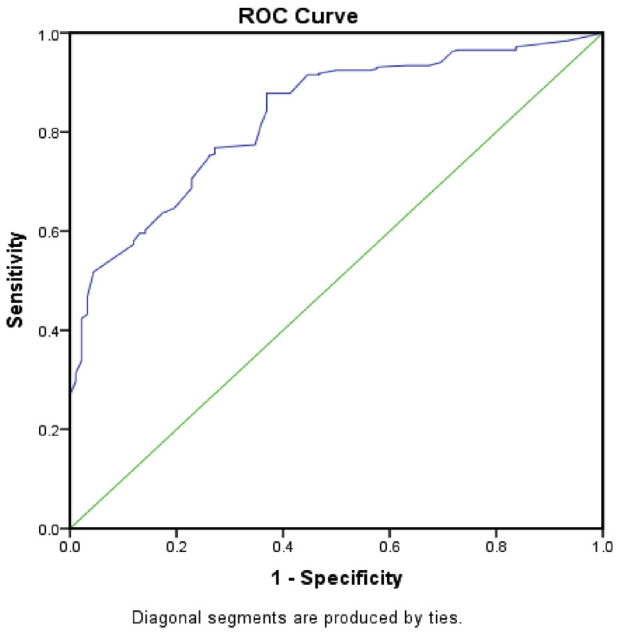

Fig. 1. ROC curve of EFT for prediction of significant CAD.

Multivariate analysis using logistic regression method revealed EFT as an independent predictor of CAD. Table 2.

5. Discussion

In our study, EFT had a strong relationship with the presence and severity of CAD. Earlier studies[7,8] have shown an association between EFT and presence of CAD but not with severity of CAD because of inclusion of patients with minimal CAD. Minimal CAD underestimates atherosclerotic burden if <70% stenosis is present in multiple epicardial coronary arteries. Hence, we have excluded patients with minimal CAD to derive EFT cut-off for predicting significant CAD. Gensini score, a better quantitative tool was used to assess CAD severity. A similar observation was seen in other studies.[4,9–11]

EFT was associated with conventional risk factors like age, diabetes mellitus, hypertension, waist circumference, smoking and alcohol use. EFT had no association with dyslipidemia and BMI corroborating the findings in other studies that visceral adiposity is more important than total adiposity for cardiovascular risk.[9,12]

In our study, EFT cut-off ≥ 4.75 mm had a sensitivity of 87% and specificity of 63% for predicting CAD. However, a cut-off ≥5.2 mm had a better predictive probability of DVD and TVD. Studies conducted in different populations have reported EFT cut-offs ranging from 4.65 to 5.2 mm to predict significant CAD.[8,10,11,13,14] Variation in EFT cut-off value could be due to ethnic differences, influencing

Table 2
Multivariate logistic regression analysis for the prediction of Coronary Artery Disease.

Parameter	Odds Ratio	95% CI	*p*-Value
Age	0.97	0.86–1.08	0.59
Gender	1.10	0.13–9.04	0.92
Type 2 Diabetes Mellitus	0.38	0.08–1.79	0.22
Hypertension	2.08	0.45–9.58	0.34
Waist Circumference	1.40	0.01–0.117	0.01
Dyslipidemia	0.93	0.13–6.6	0.94
Smoking	0.41	0.04–3.77	0.43
Alcohol use disorder	1.14	0.66–1.96	0.63
Systolic EFT ≥ 4.75 mm	4.46	3.09–6.44	<0.0001

traditional risk factors and technique of EFT measurement. EFT is best measured at end-systole because it is compressed in end diastole.[5]

Multivariate regression analysis has revealed EFT as an independent predictor of CAD over other conventional risk factors. A similar observation was seen in other studies.[9,14] Our study findings corroborate with literature from west and other parts in terms of correlation between EFT and severity of CAD except for the cut-off value to predict CAD. Epicardial fat volume assessed by cardiac CT when added to conventional risk factors and coronary calcium score offered a more accurate and effective estimation for pretest probability of CAD.[15] Future studies are required to validate pretest probability model adding EFT to conventional risk factors for prediction of CAD. EAT is a 3-dimensional structure and 2D Echocardiography may not accurately measure epicardial adiposity. The findings in our study cannot be generalised since other parts may behave differently. Hence reproducibility has to be ascertained.

6. Conclusion

In this small pilot study, EFT measured by echocardiography correlated with the presence and severity of CAD in a select subgroup of patients. However, this will require validation in larger studies.

Declaration of Competing Interest

All authors have none to declare.

References

1. Iacobellis G, Corradi D, Sharma AM. Epicardial adipose tissue: anatomic, biomolecular and clinical relationships with the heart. *Nat Clin Pract Cardiovasc Med*. 2005 Oct;2(10):536–543.
2. Rabkin SW. Epicardial fat: properties, function and relationship to obesity. *Obes Rev*. 2007 May;8(3):253–261.
3. Ahn SG, Lim HS, Joe DY, et al. Relationship of epicardial adipose tissue by echocardiography to coronary artery disease. *Heart*. 2008 Mar 1;94(3):e7.
4. Meenakshi K, Rajendran M, Srikumar S, Chidambaram S. Epicardial fat thickness: a surrogate marker of coronary artery disease–Assessment by echocardiography. *Indian Heart J*. 2016 May 1;68(3):336–341.
5. Iacobellis G, Willens HJ. Echocardiographic epicardial fat: a review of research and clinical applications. *J Am Soc Echocardiogr*. 2009 Dec 1;22(12):1311–1319.
6. Gensini GG. A more meaningful scoring system for determining the severity of coronary heart disease. *Am J Cardiol*. 1983;51:606.
7. Yañez-Rivera TG, Baños-Gonzalez MA, Ble-Castillo JL, Torres-Hernandez ME, Torres-Lopez JE, Borrayo-Sanchez G. Relationship between epicardial adipose tissue, coronary artery disease and adiponectin in a Mexican population. *Cardiovasc Ultrasound*. 2014 Dec 1;12(1):35.
8. Mustelier JV, Rego JO, González AG, Sarmiento JC, Riverón BV. Echocardiographic parameters of epicardial fat deposition and its relation to coronary artery disease. *Arq Bras Cardiol*. 2011 Aug;97(2):122–129.
9. Erkan AF, Tanindi A, Kocaman SA, Ugurlu M, Tore HF. Epicardial adipose tissue thickness is an independent predictor of critical and complex coronary artery disease by Gensini and syntax scores. *Tex Heart Inst J*. 2016 Feb;43(1):29–37.
10. Eroglu S, Sade LE, Yildirir A, et al. Epicardial adipose tissue thickness by echocardiography is a marker for the presence and severity of coronary artery disease. Nutrition, metabolism and cardiovascular diseases. 2009 Mar 1;19(3):211–217.
11. Sinha SK, Thakur R, Jha MJ, et al. Epicardial adipose tissue thickness and its association with the presence and severity of coronary artery disease in clinical setting: a cross-sectional observational study. *J Clin Med Res*. 2016 May;8(5):410.
12. Iacobellis G, Ribaudo MC, Assael F, et al. Echocardiographic epicardial adipose tissue is related to anthropometric and clinical parameters of metabolic syndrome: a new indicator of cardiovascular risk. *J Clin Endocrinol Metabol*. 2003 Nov 1;88(11):5163–5168.
13. Abd El-Aziz WF, Ahmed MK, Badr WA. Association of echocardiographic epicardial fat with the extent of coronary artery disease. *Menoufia Med J*. 2017 Jul 1;30(3):842.
14. Verma B, Katyal D, Patel A, Singh VR, Kumar S. Relation of systolic and diastolic epicardial adipose tissue thickness with presence and severity of coronary artery disease (The EAT CAD study). *J Fam Med Prim Care*. 2019 Apr;8(4):1470.
15. Zhou J, Chen Y, Zhang Y, et al. Epicardial fat volume improves the prediction of obstructive coronary artery disease above traditional risk factors and coronary calcium score. *Circ Cardiovasc Imag*. 2019 Jan;12(1), e008002. https://doi.org/10.1161/CIRCIMAGING.118.008002.