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Original Research Article

CORRELATION OF EPICARDIAL FAT THICKNESS AND SEVERITY OF CORONARY ARTERY DISEASE AS ASSESSED BY SYNTAX SCORE ON CORONARY ANGIOGRAPHY

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Abstract: *This study aimed to investigate the correlation between epicardial fat thickness and the severity of coronary artery disease (CAD) as assessed by the Syntax score on coronary angiography. A total of 50 patients with stable ischemic heart disease and uncontrolled anginal symptoms, presenting at the Cardiac Centre, Bahawal Victoria Hospital, Bahawalpur, were included in this study. These patients underwent coronary angiography, and those diagnosed with CAD were enrolled. Trans-thoracic echocardiography was performed to measure epicardial fat thickness. CAD severity was quantified using the Syntax score. Demographic data and other relevant variables were recorded in a pre-designed proforma, and data analysis was carried out using SPSS. The mean age of the study population was 51.2±9.05 years, with 54% of the participants being female. The study revealed a positive correlation between epicardial adipose tissue and the severity of CAD as assessed by the Syntax score (r = 0.426, p-value 0.002). In conclusion, this study found a positive albeit weak correlation between epicardial fat thickness and the severity of CAD as determined by the Syntax score on coronary angiography. These findings provide valuable insights into the potential role of epicardial fat as a marker for CAD severity. Further research is warranted to explore this relationship in larger and more diverse patient populations and to establish its clinical implications.*

Keywords: Epicardial fat, Epicardial adipose tissue, SYNTAX score, Severity of coronary artery disease. Echocardiography

Introduction

Increased fats in body are considered an essential risk factor that increases cardiovascular disease risk. Traditionally, obesity has been seen as a risk factor, but it is now known that fats in the body are of different characteristics; they are different in their properties of lipolysis , insulin sensitivity, ability to secrete different inflammatory markers, and thus, in their property to produce atherosclerosis (Christensen et al., 2020). In the past, the fats were considered inert and benign and acted mainly as a storage organ for excess energy in the form of triglycerides with only the function of forming or breaking down excess fats into free fatty acids and glycerol based on body metabolism and energy requirements. Recently, the fat is known to be metabolically active and interacts with various body organs.(Neeland et al., 2018) Epicardial fat (EF) is classified as visceral fat and is present between the myocardial and visceral layer of the pericardium of heart. Human EF comprises fat cells, stromo-vascular cells, few neural cells, and immune system cells.
EF is commonly found in the grooves between atria and ventricles and between ventricles but it may be present over the surface of the heart and cover 80%. Therefore, EF may affect the blood flow in the coronary artery and myocardium and its contractions (Sinha et al., 2016). According to morphology, immune-staining, physiological properties, and origin from embryo lines, there are three different types of fats in humans the white adipose tissue (WAT), the brown adipose tissue (BAT), and a third one recently known as brown-in-white AT. Many researchers have found visceral fats are more closely associated with CAD than other fats in the body (Antonopoulos and Antoniades, 2017) (Ruscica et al., 2017). EF acquires some of the properties of white fats , whose tendency to lipolysis results in the release of fatty acids and promote inflammatory cells to accumulate resulting in potential to initiate atherosclerosis in the coronaries (Madonna et al., 2019).
Numerous clinical researches have established a close relationship between the epicardial adipose tissue (EAT) and CAD. Some researches measures EAT as volume or thickness. Different methods assess it. Thickness is measured by echocardiography, CT and MRI. EAT assessed by echocardiography also correlates with carotid intima media thickness (IMT). Studies have shown positive correlation of EAT for cardiovascular disease in high risk patients (Natale et al., 2009).
Various pathophysiological processes theoretically link EAT and CAD. In 1956 Burnsides and colleagues postulated the first hypothesis of a contributory function of the EAT in the atherosclerotic process in coronaries. They observed that the lesions within coronary arteries are located at sites where EAT was present, while coronary segments within the myocardium are spare of disease. (Jc, 1956) Later, their observations were confirmed. At these particular sites inflammation and oxidised LDL receptors are found. These receptors are absent in intramyocardial coronary segments (Synetos et al., 2018). Additionally, compared to subcutaneous adipose tissue, the EAT analysis obtained by surgeons reveal increased inflammation and cytokines. The pro-inflammatory properties were not related to other factors responsible for them like obesity

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and diabetes. Adiponectin which is athero- protective is found less in the EAT.(Mazurek et al., 2003) Regardless of the conventional CV risk factors, it is found that volume of fats on the epicardial surface is also correlated with acute coronary events and is an independent factor (Eren et al., 2021).

TTE has an advantage over CT and MRI for measurement of EAT because of its easy availability, low cost, high reproducibility, and lack of radiation risk. Severity of CAD is assessed by either SYNTAX (Erkan et al., 2016; Shambu et al., 2020). Patients with metabolic syndrome have high EAT and are associated with increased risk of heart disease resulting in increased adverse outcomes (Erkan et al., 2016).

As EF thickness measurement is a non-invasive modality, its low cost and easy reproducibility will help identify high-risk patients and initiate diagnostic and preventive strategies at earlier stages. Until now, this modality has not been included in the American Heart Association or European Society of Cardiology guidelines as a standard of care. By preventing morbidity in this population group, we could unload a lot of burden on the healthcare system and improve patient's quality of life, resulting in physical, mental, and social well-being. So, the aim was to study the correlation between epicardial fat thicknesses and CAD severity to fill the potential gap in the existing sea of knowledge. Hopefully, this modality may help us predict the presence of disease and adverse events at earlier stages. Thus the objective f the study was to determine the correlation of epicardial fat thickness and CAD severity as assessed by Syntax score on coronary angiography.

Methodology

This cross sectional study was conducted in Cardiac centre, Bahawal Victoria Hospital, Bahawalpur between 01-01-2022 to 30-06-2022. Permission was taken from institutional ethical review committee. A total of 50 patients of either gender between 25 and 70 years of age were enrolled by non-probability consecutive sampling. All patients have stable ischemic heart disease with uncontrolled anginal symptoms. Sample size was calculated using PASS 2021 (Power Analysis & Sample Size), version 21.0.3 sample size calculator for Spearman's rank correlation test using Alpha value 0.05, Power 90%, and correlation coefficient under alternate hypothesis r1 = 0.523.(Eren et al., 2021). Calculated minimum sample size was 40. Considering the dropout-inflated sample size assessed by PASS 2021, 50 patients were enrolled. Informed written consent was taken from the patients. The following patients were excluded from the study: Patients with a history of diabetes mellitus, previous coronary artery bypass graft surgery (CABG), previous percutaneous coronary intervention, valvular pathology or chronic kidney disease patients, obese patients having BMI ≥ 30 kg/m2, and patients with chest deformity, chronic lung disease, poor echogenic window and patients having pleural or pericardial effusion. Patients of acute coronary syndrome were also excluded from the study. All of them underwent coronary angiography in cardiac catheterization lab of Cardiac Centre, Bahawalpur on TOSHIBA INFINIX diagnostic X-ray apparatus MODEL CAS-830B for suspected coronary artery disease. After angiography, the severity of coronary artery disease was assessed using SYNTAX score (web-based calculator to assess and quantify CAD numerically). All these patients underwent transthoracic echocardiography by a consultant cardiologist blinded from angiography findings and measured epicardial fat thickness using the GE Healthcare Vivid E95 4D Cardiac Ultrasound Machine. In the cardiac cycle it is measured at the end of systole. 3 beats are averaged and right ventricular free wall is the preferred site. All the information including previous medical conditions like, hypertension, smoking status and demographic variables like age and gender, was noted on the pre-designed proforma. Data was analysed using IBM SPSS Version 20.0 and presented as graphs and tables. The Shapiro-Wilk test was used to assess whether the variables are normally distributed. Qualitative variables (gender, hypertension, smoking status, place of living, socioeconomic status and severity of coronary artery disease) are presented as percentage and frequency. Quantitative variables (epicardial fat thickness and age) are presented as mean ± SD. Qualitative variables were compared with the chi-square test. Spearman's rank correlation analysis (it was selected over Pearson correlation coefficient because of monotonic relationship of variables) was performed to assess the correlation between epicardial fat thickness and CAD severity. Stratification was done for age, gender, hypertension, smoking status and place of living to see their effects on outcome variables. Post stratification spearman's correlation was applied. Statistically significant level is considered when the value of $p \leq 0.05$.

Results

Data from a total of 50 patients was analyzed. The mean age of the study population was 51.24 ± 9.05 years. Among the studied population, 27 (54%) were male, and 23 (46%) were female. The majority of the included subjects were from rural areas, and coronary artery disease of moderate severity predominated. The mean thickness of epicardial adipose tissue was 2.75 ± 0.69 mm. Characteristics of the study population are summarized in Table 1. Stratification of the study variables showed that the majority of them were in the age group of 41 to 50 years, and the female population predominates in the study sample relatively. The majority were non-smokers.

Spearman's rank correlation coefficient analysis of epicardial fat thickness with the angiographic CAD severity as quantified by SYNTAX score showed a statistically significant weak positive correlation (r = 0.426, p = 0.002), as depicted in Figure 1. The chi-square test between the severity of coronary artery disease and other variables like age, gender, rural/urban, hypertension, and smoking status showed no statistically significant relationship, all $p > 0.05$. Stratification of the correlation of epicardial fat thickness and the severity of coronary artery disease concerning study confounders is depicted in Table 2-3.

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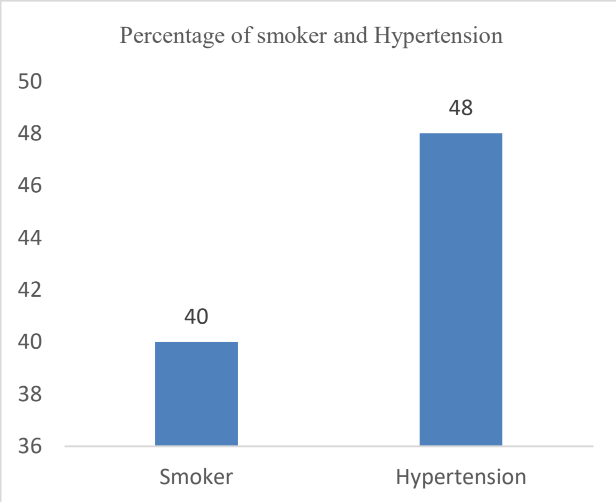

Fig.01 Percentage of Smoker and Hypertension

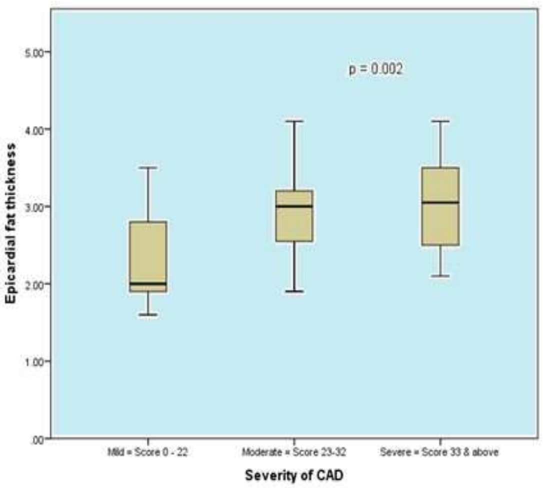

Figure 2:Box plot diagram showing the correlation of Epicardial fat thickness with the severity of

Table 1: Characteristics of the study population.

Variable	Mean	Standard deviation
Age	51.24	±9.05
Epicardial fat thickness	2.75	±0.69
Smoking pack years (n=20)	24.25	±12.06

Table 2:Stratification of Correlation of EF thickness with the severity of CAD concerning Age.

Age group	N	r	p-value
25-40 years	8	0.45	0.26
41-50 years	17	0.55	0.02
51-60 years	16	0.67	0.004
61-70 years	9	0.11	0.77

Table 4:Stratification concerning Gender, area of living, hypertension, and smoking

Gender	N	r	p-value
Male	23	0.19	0.36
Female	27	0.53	0.004
Rural	29	0.42	0.02
Urban	21	0.31	0.16
Hypertensive	24	0.50	0,01
Nonhypertensive	26	0.39	0.04
Smoker	20	0.22	0.35
Nonsmoker	30	0.55	0.002

Discussion

Our research aimed to determine the correlation between EAT and the angiographic severity of CAD assessed by SYNTAX score in patients undergoing coronary angiography for suspected CAD. We found that EAT thickness is a factor that can predict the severity of CAD. There was a statistically significant positive intensity correlation between EAT and CAD severity. The study population's age range was 36 years to 70 years, with the majority in the range of 41 to 50 years, and rural areas were predominant.

Epicardial fat is more metabolically active than abdominal fat. This tissue displays several important functions, including metabolic, mechanical, and thermogenic properties. The cytokines secreted by the epicardial adipose tissue help in myocardial modulation. EAT has a diagnostic and prognostic value (Jayawardena et al., 2021).

My study showed a statistically significant positive correlation of weak intensity between EAT and the severity of coronary artery disease on coronary angiography, r = 0.426, p = 0.00. Other studies done previously have shown similar results. A study by Eren H et al. included 430 patients and found a similar positive correlation between EAT and the severity of CAD, r = 0.523, p < 0.001. The difference between my study and Eren H et al.'s is that they included patients who presented with acute ST-elevation myocardial infarction. In contrast, in my study, we included patients with stable ischemic heart disease. The CAESAR registry, enrolling 2299 people, found a positive correlation between calcified CAD and EAT. even adjusting for other CAD risk factors (OR 2.023, 95% CI 1.282-3.193), like the findings documented in my study (Kim et al., 2017). Stratification based on age revealed extreme ages were not statistically significant, while the age group 41-50 years and 51-60 years significantly correlated with EAT, r = 0.55, p = 0.02 and r = 0.67, p = 0.004, respectively. Similar findings were documented by Shetty et al., r = 0.559, p <0.001 (Shetty et al., 2012).

Several studies have demonstrated the association of epicardial adipose tissue thickness with the severity of coronary artery disease. Sinha et al. revealed mean EF thickness in the coronary artery disease (CAD) group was more than in the non-CAD group, 5.10 ± 1.06 mm versus 4.36 ± 1.01 mm (p=0.003). The population in their study was in the age group of 51 – 60 years, while in our study, most participants were 41 – 50. In my study, the patients were stable, while 85% of their patients had suffered from

acute coronary events. Higher EF thickness was associated with more severe and multivessel disease. ROC analysis showed EF thickness > 4.65mm had 71.6% sensitivity and 73.1% specificity for predicting significant CAD. Similar to this study, another study revealed EAT volume quantified by CT was positively associated with coronary artery calcium (OR 1.21, 95% CI 1.005-1.46, p=0.04) (Rosito et al., 2008).
Slightly different from my findings of moderate correlation, Erkan AF et al. documented a strong positive correlation with CAD severity, r = 0.42 versus r = 0.82, respectively. Erkan AF et al. also documented that progressive EF thickness was associated with a significant rise in the mean Gensini and Syntax scores (p<0.001).
As in our study, another study by Gökdeniz and colleagues found EAT thickness significantly correlated to SYNTAX score (r =0.629; P <0.001). In another study by Wang et al., the association of EAT thickness determined by TTE was correlated with CAD severity, p < 0.01 (Wang et al., 2014). Contrary to our findings, Yanez R et al. found no association. The method used to evaluate the CAD severity might be responsible for this discrepancy. They used the number of coronary artery disease segments to correlate with the severity of CAD. At the same time, we used the SYNTAX score, which is more quantitative and showed a significant correlation between EAT and SYNTAX score (Yañez-Rivera et al., 2014). Lastly, further research can help strengthen this association further.

Conclusion

This study concluded that the epicardial fat correlates with CAD's angiographic severity. Although the correlation is weak, the finding is important in many ways. This non-invasive, cost-effective, and easily reproducible measure might be a surrogate marker of coronary artery disease. CAD can be predicted by measuring epicardial fat thickness.

Declarations

Data Availability statement
All data generated or analyzed during the study are included in the manuscript.
Ethics approval and consent to participate
Approved by the department concerned.
Consent for publication
Approved
Funding
Not applicable

Conflict of interest

The authors declared the absence of a conflict of interest.

Author Contribution

NAUMAN ALI (Assistant Professor)
Coordination of collaborative efforts.
MUHAMMAD IRFAN (Assistant Professor)
Conception of Study, Development of Research Methodology Design, Study Design,, Review of manuscript, final approval of manuscript
ANWAR UL HASSAN (Assistant Professor)
Manuscript revisions, critical input.
Coordination of collaborative efforts.
FOUZIA GOHAR (Assistant Professor)
Data acquisition and analysis.
NORMAN NAZEER (Medical Officer)
Data entry and Data analysis, drafting article
Data acquisition and analysis.

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