

Comparison of Epicardial Fat Volume between Patients with Normal Perfusion and Reversible Perfusion Abnormalities on Myocardial Perfusion Imaging

Abstract

Purpose of the Study: Our study purpose was to compare the epicardial fat volume (EFV) in myocardial perfusion imaging single photon emission computed tomography/computed tomography (MPI SPECT/CT) with normal and abnormal perfusion in patients with known or suspected coronary artery disease (CAD). **Materials and Methods:** one hundred and seventy-six patients (88 records with normal and 88 with reversible perfusion defects) underwent physical or adenosine stress with Tc-99m MIBI followed by SPECT and low-dose CT for attenuation correction. Rest MPI was done in patients showing perfusion defects on stress imaging. Software-based quantification of EFV was done by manually delineating pericardial contours with epicardial fat threshold set between -30 HU and -190 HU. **Results:** Median EFV in scans with normal perfusion was found to be 74.46 ml (32.92–211.51), and with reversible ischemia was 92.94 ml (43.70–207.53) with a median-summed difference score (SDS) of 5.00 (1.0–27). In 15 scans with reversible perfusion defects associated with infarcts in other segments, median EFV was 101.71 ml (63.03–156.46) with mean - SDS of 7.50 (standard deviation = 6.20). Scans with reversible perfusion defects demonstrated an increased EFV (median - 92.94 ml) when compared to scans with a normal perfusion (median = 74.64 ml) ($P < 0.001$). **Conclusion:** Our results demonstrated an increased EFV in scans with presence of active reversible ischemia compared to that of normal perfusion on MPI ($P < 0.001$) suggesting potential role of cardiac SPECT/CT to evaluate EFV for risk stratification of suspected CAD.

Keywords: Coronary artery disease, epicardial fat volume, myocardial perfusion imaging, single photon emission computed tomography/computed tomography

Introduction

Cardiovascular disease was found to be the leading cause of morbidity and mortality in India with a prevalence of 7%–13% in the urban population and 2%–7% in the rural population.^[1-4] This can be attributed to the high prevalence of the risk factors like blood cholesterol and triglyceride levels, diabetes mellitus, hypertension, smoking, alcoholism, obesity and lack of adequate physical activity etc., which are independently found to increase epicardial fat volume (EFV) around the heart. This epicardial fat is a source of proinflammatory cytokines which is involved in the formation of atherosclerosis of the coronary arteries and eventual myocardial infarction (MI).^[5-7]

Myocardial perfusion imaging single photon emission computed tomography/computed tomography (MPI SPECT/CT) is commonly used for risk stratification

or evaluation in cases with suspected or known coronary artery disease (CAD).^[8] The myocardial uptake of tracer in SPECT images is proportional to the myocardial blood flow, and acquisition of coregistered low-dose CT scan is useful for attenuation correction purposes. Considering EFV as an independent risk factor for the presence of CAD, the gold standard for measuring the EFV is CT and magnetic resonance imaging (MRI), which are relatively expensive with significant radiation exposure (in case of CT) and also require substantial expertise.^[5,9] Low-dose CT scan that is acquired as a standard protocol in MPI SPECT/CT can be used for the calculation of EFV with no additional radiation exposure or expense of money to the patient.

Many studies have shown positive correlation between increased EFV and atherosclerosis of the coronary arteries and

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plaque burden.^[7,8] However, there are no studies in India showing the association between the EFV and presence of MPI scan abnormalities in patients with suspected and known CAD. Our current study aims at comparing EFV between patients with normal perfusion and patients with the reversible perfusion abnormalities on MPI study performed in patients with suspected and known CAD.

Materials and Methods

Study population

This record-based cross-sectional analytical study consists of 176 scan records of patients who had undergone MPI between the period of January 2017 to December 2017 (age 54.27 ± 12.28 years with male to female ratio of about 2:1). The indication for the MPI procedure was either the clinical suspicion of CAD or known CAD for assessment of stress induced ischaemia. All the patients underwent ^{99m}Tc-Sestamibi MPI by SPECT with low-dose, noncontrast cardiac CT for attenuation correction purpose (SPECT/CT).

A total of 176 stress MPI scan records were reviewed, 88 were with normal perfusion and 88 having abnormal myocardial perfusion on the MPI scans. Records were included consecutively with only exclusion criterion being the bad image quality [Figure 1].

Retrospectively, the patient database was analysed for the history of smoking, alcohol consumption, presence of diabetes, hypertension, hyperlipidemia, previous history of MI, presence of CAD on CT angiography and family history of MI. Height and weight of the patients in the records were collected for measuring body mass index (BMI). The study was conducted after the approval of protocol by Institute Ethics Committee (JIP/IEC/2018/065).

Single photon emission computed tomography nuclear perfusion imaging

The records collected for analysis included patients who underwent exercise testing which was performed in standardised treadmill exercise protocol (in either Bruce or Modified-Bruce protocol) or using pharmacological testing with intravenous adenosine infusion (at the rate of $140 \mu\text{g}/\text{kg}/\text{min}$ for 6 min) in patients who were unable to perform treadmill stress test.^[10] The injection of Tc-99m Sestamibi was during the peak of exercise in treadmill protocol and at 3rd minute of infusion in adenosine protocol. SPECT was acquired after 30–60 min after treadmill testing and after 60 min of adenosine infusion, followed by low-dose CT for attenuation correction. The scans were acquired on SPECT/CT scanner equipped with low-energy high-resolution collimator (Symbia T6 dual-headed gamma camera, Seimens Ltd.).

In stress scans that showed perfusion defects, rest MPI had been performed in a single day as a 1-day protocol or on another day as 2-day protocol. The scans were analysed by experienced nuclear medicine physician for the presence of perfusion defects. Normal scans were defined by the absence of perfusion defects whereas abnormal scans were defined by the presence of reversible perfusion defects (ischemia) with or without the presence of associated infarcts.

Computed tomography analysis of epicardial fat volume

In all MPI scans, low-dose CT scan (at 120 kVp with tube currents of 60–70 mAs) for purpose of attenuation correction was acquired. Epicardial fat was defined as adipose tissue located inside the pericardium, which includes even peri-coronary adipose tissue. Pericardial contours were manually delineated with bifurcation of pulmonary trunk marking the upper slice limit, and the lower slice limit was just inferior to posterior descending artery. Delineation of epicardial fat within pericardium was done by drawing a region of interest (ROI) on consecutive trans-axial slices with slice thickness set at 10 mm and the threshold for epicardial fat detection set between -30 HU and -190 HU. EFV was then calculated by the Symbia T6 workstation software by multiplying the area within the ROI fulfilling the threshold parameters for epicardial fat with the slice thickness.

Statistical analysis

Analysis of the data was done using a statistical software called Statistical Package for Social Services (SPSS) version 18 (SPSS Inc., Chicago, IL, USA). The normality of data was evaluated for each continuous variable from normal distribution plots, histograms and by the Kolmogorov–Smirnov test. Mean value \pm standard deviation was reported for all continuous variables following normal distribution pattern, whereas median with inter-quartile range was reported for continuous data with nonnormal

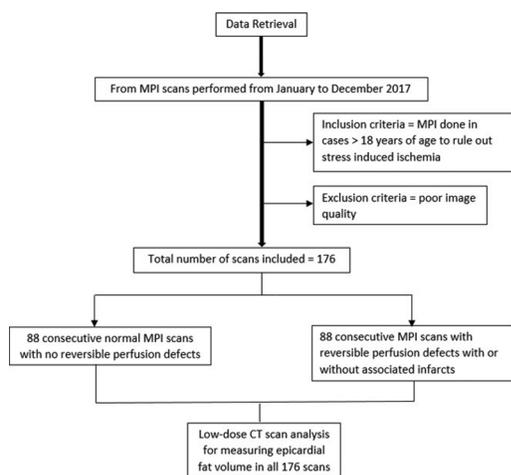


Figure 1: Flow-chart showing the inclusion of studies for data retrieval from myocardial perfusion imaging studies showing the inclusion and exclusion criteria

distribution. Categorical variables were all expressed in proportions and percentages. Significance was assessed at 5% level of significance. Since the groups included in the study are independent of each other, independent Student's *t*-test was used to calculate the significance of continuous study variables which followed normal distribution whereas Mann–Whitney U-test was used for variables not following normal distribution of data.

Results

A total of 176 records of MPI, who were evaluated for the suspicion of CAD or were a known case of CAD, were included in the study. 88 normal MPI scan records and 88 with perfusion defects were both consecutively analysed. Significant difference was noted in age with records of ischemia group being older than the cases with normal perfusion ($P < 0.001$). No significant difference was noted in BMI between both the groups ($P = 0.395$). More number of males and less females were noted in the group with ischemia compared to the group with normal perfusion. Baseline characteristics of the scan records are as described in Table 1, and represented in the Figure 2.

Image analysis

Among the normal MPI scans, one record with history of 2-year old MI in left anterior descending (LAD) territory and three records with known CAD on prior coronary angiography (one patient with approximately 30% stenosis in LAD and two patients with <40% stenosis in LAD and right coronary artery [RCA] territories each) showed no perfusion defects in the respective territories. Among 88 scan records with abnormal results on MPI, all showed reversible perfusion defects in one or more territories. Twenty-seven scans revealed perfusion defects in LAD territory, 13 in left circumflex (LCX), 24 in RCA, 5 in LAD and LCX, 7 in LAD and RCA, 11 in LCX and RCA, and 1 scan showed defect in all three major coronary artery territories. Out of these 88 records, 15 scans showed reversible ischemia associated with fixed perfusion defects (infarcts) in other segments. Among these scans, infarcts were noted in 6 scans in LAD territory, 3 in LCX, 5 in RCA, and 1 in LCX and RCA territories. The proportions of perfusion defects in LAD, LCX, and RCA territories are as depicted in Figure 3.

Table 1: Baseline characteristics

Demographics	Total number of records (176)	Normal (88)	Ischemia (88)
Age (years)	54.27±12.28	50.43±12.50	58.11±10.82
Males (%)	117 (66.5)	52 (59.09)	65 (73.9)
Females (%)	59 (33.5)	36 (40.91)	23 (26.1)
BMI (kg/m ²)	25.28±4.83	25.59±5.37	24.96±4.22

Age and BMI were represented as mean±SD, and gender was represented in percentages. SD: Standard deviation, BMI: Body mass index

Total EFV in cases with normal myocardial perfusion was 74.46 ml (range: 32.92–211.51 ml) and in scans with abnormal perfusion defects was 92.94 ml (range: 43.70–207.53 ml). Records with reversible perfusion defects showed a median SDS of 5.00 (range: 1.0–27). Records with reversible perfusion defects on myocardial perfusion imaging have demonstrated an increased total EFV compared to scans showing normal myocardial perfusion (median: 92.94 ml, range: 43.70–207.53 ml vs. median: 74.46 ml, range: 32.92–211.51 ml; $P < 0.001$). Subgroup analysis in the group with reversible perfusion defects, the 15 records which were associated with infarcts in other segments have demonstrated a mean total EFV of 102.51 ml ± 31.34 ml, with a mean SDS of 7.50 ± 6.20. The averages of EFV in patients with reversible perfusion defects distributed according to the territories involved is depicted in Figure 4, whereas comparison of EFV in scans with normal perfusion and with that of reversible perfusion defects is as depicted in Figure 5.

Discussion

Cardiovascular diseases was found to be leading cause of morbidity and mortality in developing countries like India with ever increasing prevalence of the risk factors like diabetes mellitus, hypertension, obesity etc., all of which were found to independently increase EFV which is a source of proinflammatory cytokines.^[5,7] It eventually leads to functional and morphological changes in the heart.^[11-13] Epicardial fat can be described as adipose tissue located within the pericardium of the heart extending from the bifurcation of pulmonary trunk superiorly till just inferior to posterior descending artery. There are multiple studies with mixed results in the past comparing the relationship between EFV and the presence of CAD to establish EFV as independent risk factor for CAD.^[14-16]

Measuring the EFV can be done using anatomical imaging like transthoracic ultrasound, CT and MRI all of which are either highly expertise dependent or expensive. Low-dose CT which is acquired for the purpose of attenuation correction in myocardial perfusion SPECT/CT imaging, a scan regularly done for assessing the presence of CAD, can be used for measuring EFV with relative ease and low cost compared to traditional CT and/or MRI.

Our retrospective record based cross-sectional analytical study has included 176 records (88 with normal perfusion and 88 with reversible defects on MPI) with no significant difference in mean BMI between the two groups, but the records in ischaemia were of older mean age compared to that of records with normal perfusion ($P < 0.001$). Our study demonstrated that there is increased total EFV in patients with reversible perfusion defects compared to the normal counterparts (92.94 ml, 43.70–207.53 ml vs. 74.46 ml, 32.92–211.51 ml; $P < 0.001$) [Figures 6 and 7].

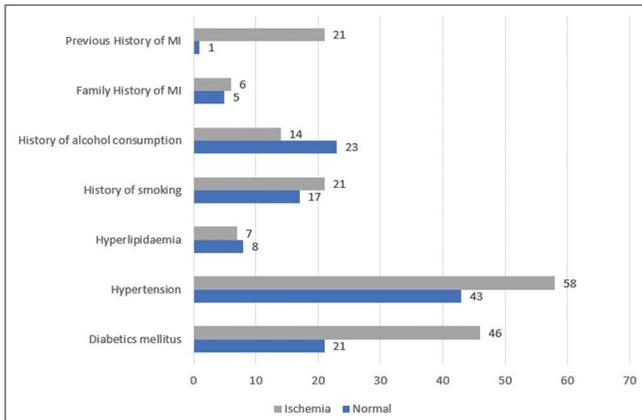


Figure 2: Demographics of risk factors. Clustered bar chart representing the number of records with respective risk factors. Ischemia/grey bars represent the number of records showing reversible perfusion abnormalities; Normal/blue bars represent records with no perfusion abnormalities on myocardial perfusion imaging study

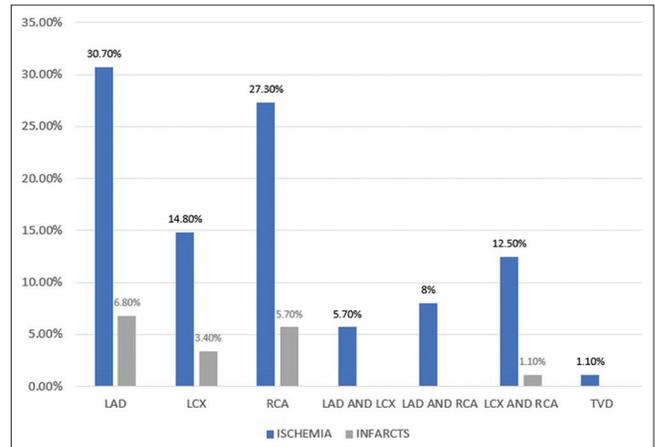


Figure 3: Clustered column chart showing percentages of perfusion defects (depicted on vertical axis) divided according to their respective territories (as depicted on horizontal axis). Perfusion defects on stress-rest myocardial perfusion imaging study are separated. Absence of grey column represents absence of infarcts in the respective territories. TVD: Triple vessel disease involving LAD, LCX and RCA vessels. LAD: Left anterior descending, LCX: Left circumflex, RCA: Right coronary artery

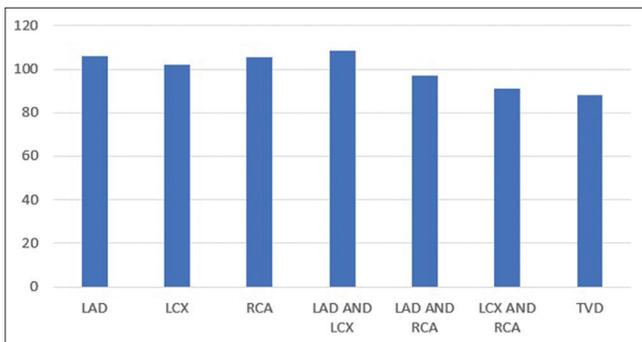


Figure 4: A simple column chart showing the average epicardial fat volumes (in ml) with respect to the perfusion defect noted in respective particular territory/territories

Our findings are in agreement with other similar studies which showed consistently increased amount of EFV in a setting of active myocardial ischemia. A previous study done by Khajawa *et al.*, showed similar results.^[6] They have prospectively included 396 patients who then underwent MPI SPECT/CT for evaluation of CAD. The investigators have measured epicardial fat parameters in low-dose CT which was acquired as a part of MPI SPECT/CT for attenuation correction. Regional epicardial fat thickness, area and total volume of epicardial adipose tissue (EAT) were analysed. They have found that the mean EFV in patients with reversible ischemia group was significantly increased ($P < 0.001$) compared to that of normal subjects with no perfusion abnormalities. Regional EFV analysis in their study revealed significantly increased epicardial fat in the territories of RCA (69.2 ± 51.5 ml in regional ischemia group vs. 46.6 ± 32.0 ml in normal group, $P = 0.03$) and also in LAD artery (87.1 ± 76.4 ml in regional ischemia vs. 46.7 ± 40.6 ml in normal controls, $P = 0.005$).

Another study done by Janik *et al.*, also showed similar results.^[17] The author has quantified EAT volume and coronary artery calcium (CAC) by analysing PIn a case-

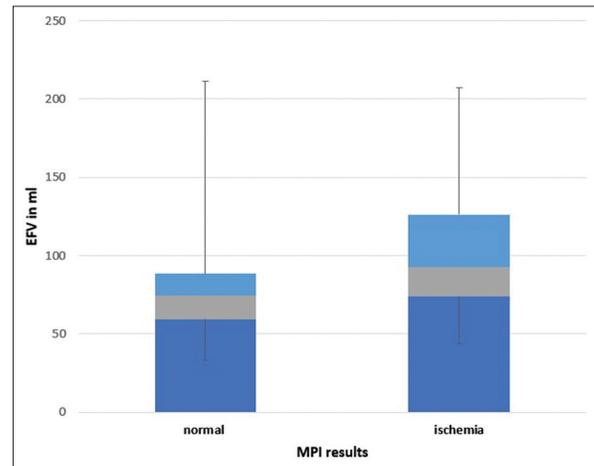


Figure 5: Box-plot diagram showing the distribution of epicardial fat volume in association with single photon emission computed tomography myocardial perfusion imaging results. Scans with evidence of ischemia on single photon emission computed tomography myocardial perfusion imaging showed a significant increase in epicardial fat volume compared to that with normal nuclear perfusion imaging ($P < 0.001$; confidence interval >95%)

control study done by Tamarappoo *et al.*, they have included a cohort of 1777 patients with no previous history of CAD.^[18] Noncontrast CT was performed in these patients for calculating coronary calcium score (CCS) which was done within 6 months of myocardial perfusion SPECT/CT. They have compared 73 cases (positive for ischemia) and 146 controls (normal perfusion scintigraphy) who were matched by age, sex, CCS, and etiological aspects of CAD. Similar to our study, the investigators have demonstrated increased pericardial fat volume in cases with ischemia when compared to controls with normal myocardial perfusion (99.1 ± 42.9 ml vs. 80.1 ± 31.8 ml; $P = 0.0003$).

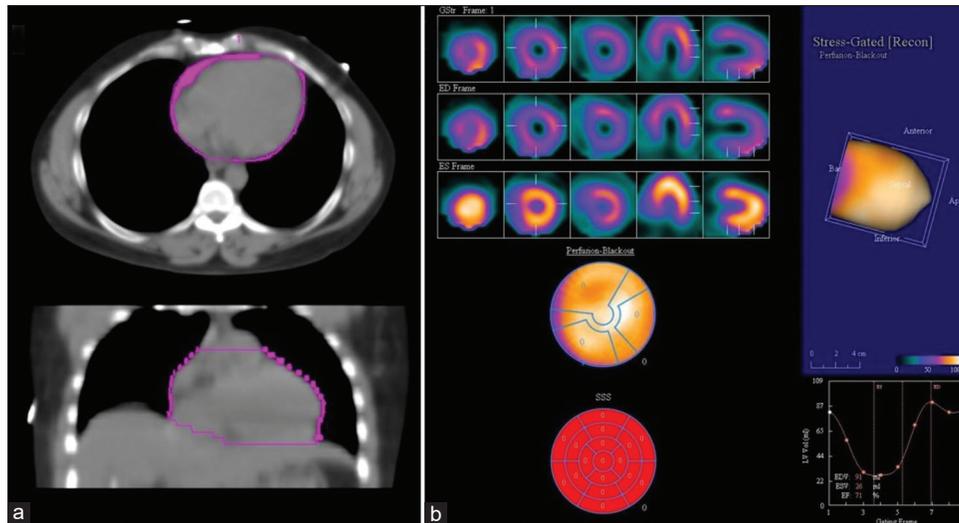


Figure 6: Scan record of a 40-year-old male patient with normal perfusion on the myocardial perfusion single photon emission computed tomography/computed tomography. The distribution of the epicardial fat is seen in transaxial and coronal planes after delineation and processing (a), and the distribution of radiotracer is seen in single photon emission computed tomography sectional images, polar plot and the gated images (b). Epicardial fat volume in this record was found to be 82.23 ml

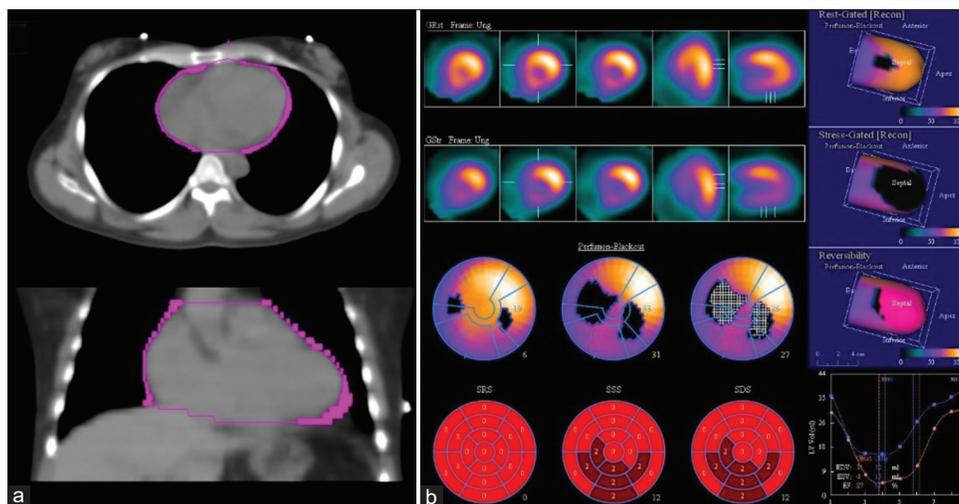


Figure 7: Scan record of a 70-year-old male patient with reversible perfusion defect on the stress and rest myocardial perfusion single photon emission computed tomography/computed tomography. The distribution of the epicardial fat is seen in transaxial and coronal planes after delineation and processing (a), and the ischemic changes in left anterior descending and left circumflex territories are seen in single photon emission computed tomography sectional images, polar plot and the gated images (b). Epicardial fat volume in this record was found to be 115.87 ml

The findings from multiple studies suggest that the increased EFV which may be related to increased expression of cytokines and adipokines are in-turn associated with noncalcified vulnerable plaque rupture,^[6,19] leading to increased risk of major coronary events.^[20] In our study, we analysed total EFV from scan records and demonstrated that there is in fact increased EFV in patients with reversible perfusion defects compared to normal patients. There are some studies showing that there may be increase in EFV with age,^[16,21,22] being as high as 22% in people more than 65 years of age,^[23] this may have been a confounding factor in our study where we found the mean age in the group with reversible ischemia to be 58.11 ± 10.82 years. However, our findings suggest that

EFV is related to the presence of CAD and is also related to other risk factors as demonstrated from prior studies. In future, our results may potentially help in assessing the risk of CAD in patients undergoing plain CT for the purpose of evaluation of diseases other than CAD.

Conclusion

The total EFV measured in records with reversible perfusion abnormalities on myocardial perfusion scintigraphy was found to be significantly higher compared to that of records showing normal perfusion. Total EFV, calculated from low-dose CT scan acquired as a part of MPI SPECT/CT for attenuation correction of SPECT

images, might be a good additional parameter to predict the presence of ischemia. Though our study has shown a significant difference in EFV between normal patients and patients with stress induced ischemia, larger prospective study with bigger sample population might be needed to confirm the results.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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