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Epicardial fat volume by dual energy CT and its correlation with coronary artery calcium scoring, HS-CRP and CIMT in predicting risk of coronary artery disease

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Abstract

Background: Coronary artery disease (CAD) is characterized by atherosclerosis in coronary arteries. CAD happens to be the leading cause of death worldwide and was reported to be responsible for death of approximately 7.2 million persons as per a WHO report published in 2004, with number of males being slightly higher as compared to that of females (3.8 million as compared to 3.4 million). Prevalence of CAD in US population aged 20 years or more is reported to be 6.7% (7.4% males, 6.2% females). Worldwide its prevalence is estimated to be approximately 5-8%.

Material and Method: This prospective observational study conducted for duration of 18 months at Era' slucknow Medical College and Hospital located at Lucknow, Uttar Pradesh. Included all the patients aged between 25 – 70 years presenting with complaints of chest pain were clinically examined, patients showing symptoms of artery diseases were subjected to radiological and biochemical examination. An informed consent for inclusion in the study was obtained, demographic information, duration and nature of complaints were recorded on a separate case sheet (Appendix). Radiological and biochemical findings were also recorded on the case sheet. Epicardial Fat volume and coronary artery calcium scoring were evaluated on Siemens somatom- Force (384 slice) Dual Energy CT. CIMT was evaluated by USG Doppler. CIMT was measured by carotid arteries imaging on VOLUSON P8, using a high frequency 7-12 MHz linear electronic array transducer. CAC score was calculated by Agatston score. HsCRP was measured by turbidimetric assay on auto-analyzer

Result: Out of 42 patients enrolled in the study, 13 (31.0%) patients were diagnosed as coronary artery disease, rest 29 (69.0%) were not diagnosed to be suffering from coronary artery disease. Range of age of patients enrolled in the study was 27 to 65 years, mean age was 46.33±10.59. Mean age of CAD patients (56.15±8.55 years; range 40-65 yrs) was significantly higher as compared to No CAD (41.93±8.25 years; range: 27-60 years).Range of Body mass Index of patients enrolled in the study was 22.00 to 33.20 kg/m2 and mean body mass index was 26.00±3.09 kg/m2. Body mass index of CAD patients (30.13±1.63; range: 28-33.20 kg/m2) was found to be significantly higher than that of No CAD patients (24.15±1.17; range: 22.0-27.0 kg/m2).Range of Epicardial fat volume (EFV) of patients enrolled in the study was 7.15 to 28.00 cc, mean EFV was 12.36±6.27 cc. Mean EFV of patients of CAD was found to be significantly higher than No CAD (15.69±7.41 vs. 10.87±5.15 cc).

Conclusion: A total of 42 patients presenting with chest pain at Department of Cardiology were enrolled. Of these 42 patients, 13 (31.0%) were confirmed to be suffering from Coronary artery disease and rest 29 (69.0%) confirmed as not suffering from Coronary artery. CAD patients were older and higher BMI than No CAD patients. Gender did not show any significant association with CAD. Correlation of EFV with Total Calcium score and hs-CRP were significant. Correlation of EFV and CIMT was not found to be significant. Total Calcium score, EFV and hsCRP were found to be significant predictors of coronary artery disease (Area under curve 0.908, 0.773 and 0.764 respectively).

Keywords: CACS, EFV and CAD

Introduction

Coronary artery disease (CAD) is characterized by atherosclerosis in coronary arteries. It is one of the biggest contributors to the group of heart and blood vessel diseases covered under the broad term cardiovascular disease (CVD) along with coronary heart disease (CHD), acute coronary syndrome (ACS) and several other conditions [1]. CAD happens to be the leading cause of death worldwide and was reported to be responsible for death of approximately 7.2 million persons as per a WHO report published in 2004, with number of males being slightly higher as compared to that of females (3.8 million as compared to 3.4 million) [2].

The burden of CAD associated mortalities is increasing continuously and has been projected to be responsible for deaths of a total of 11.1 million persons worldwide in the year 2020. In USA, coronary events in human beings are recorded at every 26 seconds, resulting in death of a person in every one minute [3]. In Europe, between 1 in 5 and 1 in 7 European women die from CAD, and the disease accounts for between 16% and 25% of all deaths in European men. Prevalence of CAD in US population aged 20 years or more is reported to be 6.7% (7.4% males, 6.2% females) [4]. Worldwide its prevalence is estimated to be approximately 5-8%. There are marked differences in the prevalence of CAD across different regions of the world, nations, and even between regions within a country [5].

The prevalence of CAD risks in Indians living in India is 11% for non-diabetic patients and 21.4% for diabetic patients. Although earlier considered to be a disease of developed world, coronary artery disease is no longer a disease of wealthy and developed nations only. Its prevalence as well as associated mortality burden is increasing in the developing countries quickly [6]. According to the Global Burden of Disease Study, the developing countries contributed 3.5 million of the total number of 6.2 million deaths from CAD in 1990. The projections estimate that these countries will account for 7.8 million of the 11.1 million deaths due to CAD in 2020. According to global and regional projections of mortality and burden of disease, CAD will remain the leading cause of death for the next 20 years [7].

It is clinically important to identify the “vulnerable patient” because the initial manifestation of CVD is sudden death in approximately one-fifth of the patients, the prognosis of those who survive a vascular event is poor, though effective primary prevention strategies are available [8]. However, it can be challenging to identify which patients will most benefit from a primary prevention strategy beyond therapeutic lifestyle change. Population based screening tools that assign a risk probability, such as the Framingham risk score (FRS) [9].

Material and Method

This prospective observational study conducted for duration of 18 months at Era’s Lucknow Medical College and Hospital located at Lucknow, Uttar Pradesh. Included all the patients aged between 25-70 years presenting with Complaints of chest pain were clinically examined, patients showing symptoms of artery diseases were subjected to radiological and biochemical examination. An informed consent for inclusion in the study was obtained, demographic information, duration and nature of complaints were recorded on a separate case sheet (Appendix). Radiological and biochemical findings were also recorded on the case sheet.

Epicardial Fat volume and coronary artery calcium scoring were evaluated on Siemens somatom- Force (384 slice) Dual Energy CT.

CIMT was evaluated by USG Doppler. CIMT was measured by carotid arteries imaging on VOLUSON P8, using a high frequency 7-12 MHz linear electronic array transducer.

Patients with chest pain under evaluation for coronary artery disease were included. The sampling frame of the study was bound by the following inclusion and exclusion criteria:

Inclusion Criteria

- Patients with chest pain who were evaluated for coronary artery disease with age group 25-70 years.
- Patients giving their consent for inclusion in the study

Exclusion Criteria

- Significant Valvular heart disease (i.e. greater than insufficiency or stenosis)
- Renal dysfunction patients.
- Haemo dynamically unstable patients
- Major systemic illness such as chronic inflammatory disease active malignancy, and other illness.

CAC score was calculated by Agatston score. Grading of coronary artery disease (based on total calcium score).

- No evidence of CAD:0 calcium score
- Minimal: 1-10.
- Mild: 11- 100.
- Severe:>400.

In this study exposure radiation is calculated by DLP (dose length product) where I DLP = 0.018 mSV. Lowest annual dose at which my increase in cancer is clearly evident is 100 msv. When coronary calcium was detected, we used an automated program based on the Agaston method to compute the CACS of all the coronary arteries.

HsCRP was measured by turbidimetric assay on auto-analyzer.

Significant coronary artery stenosis was defined as >50% reduction of the internal diameter of major epicardial arteries and side branches with a diameter ≥2.5 mm.

Data recorded on the case sheet was subjected to analysis.

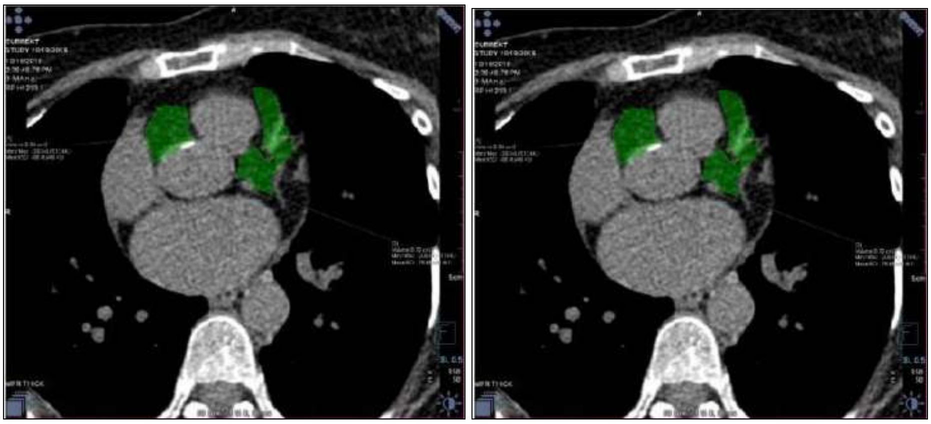


Fig 1: Axial non-contrast DECT image of heart depicting the zone ofepicardial fat along the major coronary vessels.

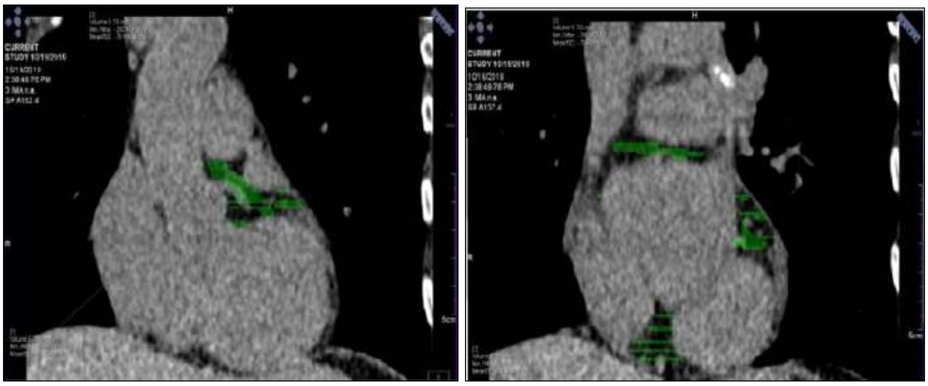


Fig 2: On coronal non-contrast DECT image of heart depicting the zone of epicardial fat along the major coronary vessels.

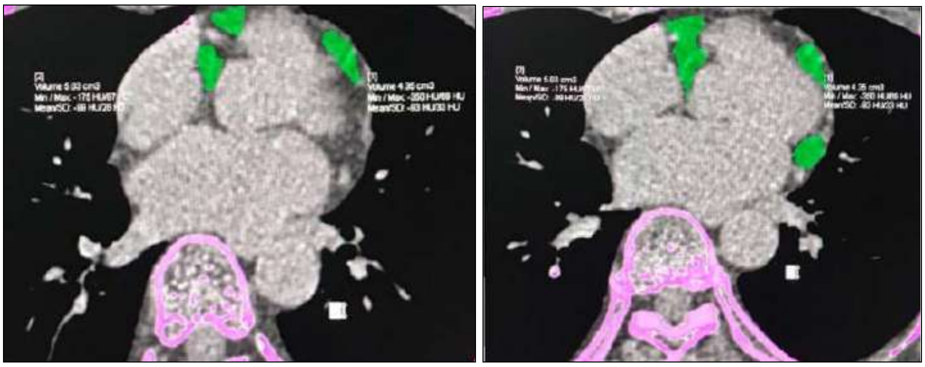


Fig 3: Axial non-contrast DECT image of heart depicting zone of epicardial fat along the major coronary vessels.

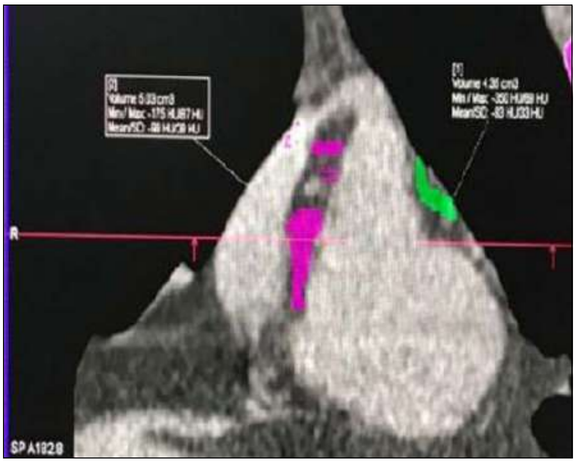


Fig 4: Saggital non contrast DECT image of heart depicting the zone of epicardial fat along the major coronary vessels.

Fig 5: Axial coronary CT image of a patient showing calcifiedplaque in LAD and RCA.

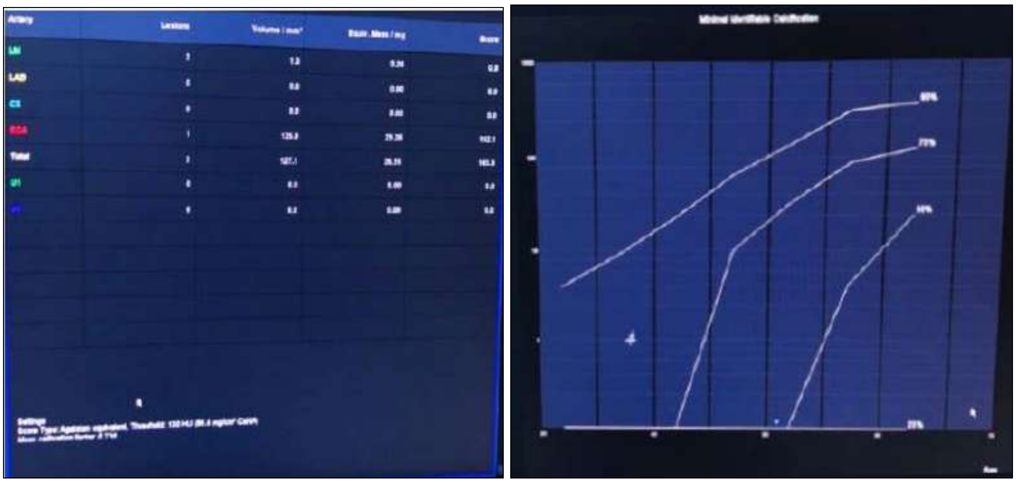


Fig 6: Coronary artery calcium scoring chart with Agatson Score and percentile graph showing identifiable calcification.

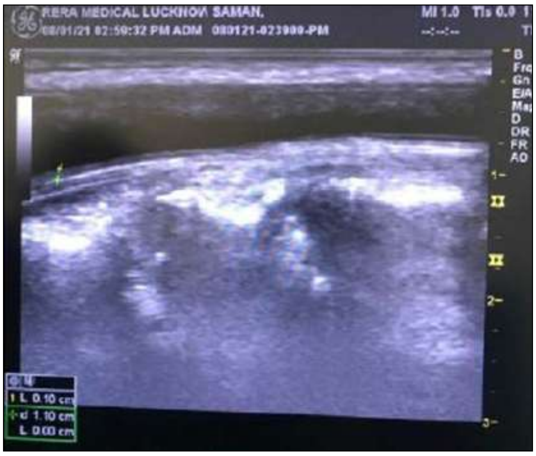


Fig 7: Gray scale image of right CCA showing raised CIMT.

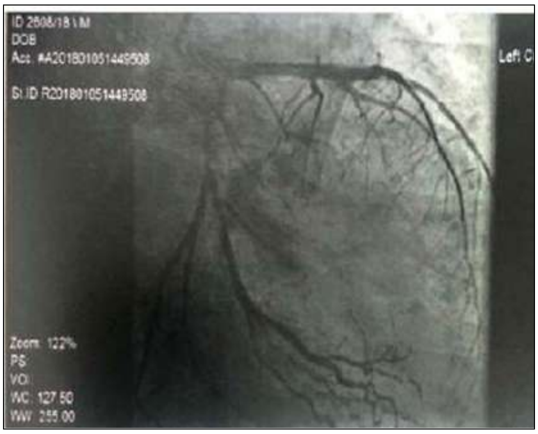


Fig 8: DSA image showing opacified LMCA, LAD and LCX with presence of significant stenosis in proximal part of LCX.

Fig 9: CT angiography VRT image showing normal coronary arteries with no obstruction.

Results

Table 1: Distribution of cases according to findings of Coronary Artery Angiography

SN	Coronary angiography findings	No. of cases	Percentage
1-	No coronary artery disease	29	69.0
2-	Coronary artery disease	13	31.0
		42	100.0

Out of 42 patients enrolled in the study, 13 (31.0%) patients were diagnosed as coronary artery disease, rest 29 (69.0%) were not diagnosed to be suffering from coronary artery disease.

Table 2 shows comparison of Age of patients with and without CAD.

Table 2: Comparison of Age (years) of cases with and without CAD

Status	No.	Min.	Max.	Mean	S.D.
No CAD	29	27	60	41.93	8.25
CAD	13	40	65	56.15	8.55
Total	42	27	65	46.33	10.59

't'=5.108; p<0.001

Range of age of patients enrolled in the study was 27 to 65 years, mean age was 46.33±10.59. Mean age of CAD patients (56.15±8.55 years; range 40-65 yrs) was significantly higher as compared to No CAD (41.93±8.25 years; range: 27-60 years).

Table 3: Comparison of Gender of cases with and without CAD

SN	Gender	No CAD (n=29)		CAD (n=13)		Total (n=42)	
		No.	%	No.	%	No.	%
1-	Female	14	48.3	4	30.8	18	42.9
2-	Male	15	51.7	9	69.2	24	57.1

χ^2=1.123 (df=1); p=0.289

Out of 42 patients enrolled in the study, 18 (42.9%) were females and rest 26 (57.1%) were males. Though proportion of males was higher among CAD patients as compared to No CAD (69.2% vs. 51.7%) but this difference was not found to be significant statistically.

Table 4: Comparison of Habitat of cases with and without CAD

SN	Habitat	No CAD (n=29)		CAD (n=13)		Total (n=42)	
		No.	%	No.	%	No.	%
1-	Rural	9	31.0	3	23.1	12	28.6
2-	Urban	20	69.0	10	76.9	30	71.4

χ^2=0.279 (df=1); p=0.598

Majority of the overall (71.4%) as well as CAD and No CAD patients belonged to urban areas (69.0% & 76.9%), rest belonged to rural areas. Though proportion of patients from rural areas was lower among CAD as compared to No CAD patients (23.1% vs. 31.0%) but this difference was not found to be significant statistically.

Table 5: Comparison of Body weight (kg) of cases with and without CAD

CAD Status	No.	Min.	Max.	Mean	S.D.
No CAD	29	63	88	77.86	7.13
CAD	13	84	105	97.05	5.61
Total	42	63	105	83.80	11.16

't'=8.570; p<0.001

Body weight of CAD patients (97.05±5.61 kg; range: 84-105) was found to be significantly higher than that of No CAD patients (77.86±7.13 kg).

Table 6: Comparison of Body Mass Index (kg/m^2) of cases with and without CAD

CAD Status	No.	Min.	Max.	Mean	S.D.
No CAD	29	22.00	27.00	24.15	1.17
CAD	13	28.00	33.20	30.13	1.63
Total	42	22.00	33.20	26.00	3.09

't'=13.518; p<0.001

Range of Body mass Index of patients enrolled in the study was 22.00 to 33.20 kg/m^2 and mean body mass index was 26.00±3.09 kg/m^2. Body mass index of CAD patients (30.13±1.63; range: 28-33.20 kg/m^2) was found to be significantly higher than that of No CAD patients (24.15±1.17; range: 22.0-27.0 kg/m^2).

Table 7: Comparison of Occupation of cases with and without CAD

SN	Occupation	No CAD (n=29)		CAD (n=13)		Total (n=42)	
		No.	%	No.	%	No.	%
1-	Housewife	13	44.8	2	15.4	15	35.7
2-	Retired	2	6.9	4	30.8	6	14.3
3-	Service*	8	27.6	3	23.1	11	26.2
4-	Businessman	5	17.2	4	30.8	9	21.4
5-	Student	1	3.4	0	0.0	1	2.4

χ^2=7.044 (df=4); p=0.134
*Teacher/ Police/Doctor

Proportion of CAD patients was higher as compared to No CAD occupied as Retired (30.8% vs. 6.9%) and Businessman (30.8% vs. 17.2%) while for rest of the occupations proportion of No CAD patients was higher as compared to CAD i.e. Housewife (44.8% vs. 15.4%), Service (27.6% vs. 23.1%) and Student (3.4% vs. 0.0%). Association of occupation and CAD was not found to be significant statistically.

Table 8: Comparison of Risk factors among cases with and without CAD

SN	Risk factors	Total (n=42)	No CAD (n=29)		CAD (n=13)		Chi-square	
			No.	%	No.	%	χ^2	'p'
1-	Diabetes	10	5	17.2	5	38.5	2.228	0.136
2-	Hypertension	20	9	31.0	11	84.6	10.331	0.001
3-	Smoking	5	2	6.9	3	23.1	2.241	0.134
4-	Family h/o CAD	12	7	24.1	5	38.5	0.902	0.342
5-	H/o Sun exposure	42	29	100.0	13	100.0	–	–
6-	Dietary intake of dairy products	42	29	100.0	13	100.0	–	–
7-	Daily exercise habit	14	10	34.5	4	30.8	0.056	0.813

All the patients enrolled in the study had history of Sun Exposure and dietary intake of dairy products. Habit of Daily exercise was found to be lower in CAD patients as compared to No CAD patients (30.8% vs. 34.5%), this difference was not found to be significant.
Proportion of CAD patients was higher as compared to No CAD suffering from Diabetes (38.5% vs. 17.2%), Hypertension (84.6% vs. 31.0%), Family history of CAD (38.5% vs. 24.1%) and Habit of smoking (23.1% vs. 6.9%). Only risk of hypertension was found to be significantly associated with CAD.

Table 9: Comparison of Hemodynamic parameters of cases with and without CAD

SN		No CAD (n=29)		CAD (n=13)		Student 't' test	
		Mean	SD	Mean	SD	't'	'p'
1-	Heart rate (beats/min)	81.45	4.51	81.31	4.91	0.091	0.928
2-	Systolic BP (mm Hg)	127.52	11.09	134.77	8.96	-2.069	0.045
3-	Diastolic BP (mm Hg)	82.90	8.58	87.38	5.97	-1.705	0.096

Difference in heart rate of CAD and No CAD patients (81.31±4.91 vs. 81.45±4.51 beats/min) was not found to be significant. Systolic BP of CAD patients was found to be significantly higher than No CAD patients (134.77±8.96 vs. 127.52±11.09 mm Hg). Though diastolic BP of CAD patients was found to be higher than that of No CAD (87.38±5.97 vs. 82.90±8.58 mm Hg) but this difference was not found to be significant statistically.

Table 10: Comparison of Biochemical/Lipid parameters of cases with and without CAD

SN	Parameter	No CAD (n=29)		CAD (n=13)		Student 't' test	
		Mean	SD	Mean	SD	't'	'p'
1-	HbA1c (%)	5.66	0.89	6.97	0.18	-5.239	<0.001
2-	hsCRP (mg/L)	3.17	0.80	4.32	1.85	-2.861	0.007
3-	S Uric Acid (mg/dl)	0.78	0.27	0.89	0.25	-1.260	0.215
4-	Total Cholesterol (mg/dl)	205.38	36.70	238.48	7.43	-3.202	0.003
5-	Triglycerides (mg/dl)	198.62	48.43	283.54	27.71	-5.879	<0.001
6-	HDL (mg/dl)	41.75	14.80	38.17	14.05	0.736	0.466
7-	LDL (mg/dl)	135.01	42.05	172.02	6.75	-3.134	0.003

CAD patients as compared to No CAD patients had significantly higher HbA1c (6.97±0.18 vs. 5.66±0.89%), hs-CRP levels (4.32±1.85 vs. 3.17±0.80 mg/L), Total Cholesterol (238.48±7.43 vs. 205.38±36.70 mg/dl), Triglyceride level (283.54±27.71 vs. 198.62±48.43 mg/dl) and LDL levels (172.02±6.75 vs. 135.01±42.05 mg/dl).

CAD and No CAD patients had comparable S. Uric acid (0.89±0.25 &0.78±0.27 mg/dl) and HDL (38.17±14.05 & 41.75±14.80 mg/dl).

Table 11: Comparison of Epicardial fat volume (cc) of cases with and without CAD

CAD Status	No.	Min.	Max.	Mean	S.D.
No CAD	29	7.15	27.00	10.87	5.15
CAD	13	8.00	28.00	15.69	7.41
Total	42	7.15	28.00	12.36	6.27

‘t’=2.436; p=0.019

Range of Epicardial fat volume (EFV) of patients enrolled in the study was 7.15 to 28.00 cc, mean EFV was 12.36±6.27 cc. Mean EFV of patients of CAD was found to be significantly higher than No CAD (15.69±7.41 vs. 10.87±5.15 cc).

Table 12: Comparison of CIMT (mm) of cases with and without CAD

CAD Status	No.	Min.	Max.	Mean	S.D.
No CAD	29	0.5	1.0	0.77	0.11
CAD	13	0.7	1.0	0.81	0.10
Total	42	0.5	1.0	0.78	0.11

‘t’=1.074; p=0.289

Though mean CIMT thickness of CAD patients (0.81±0.10; range: 0.7-1.0 mm) was higher as compared to that of No CAD patients (0.77±0.11; range: 0.5-1.0 mm), but this difference was not found to be significant statistically.

Table 13: Comparison of Total Calcium score of cases with and without CAD

CAD Status	No.	Min.	Max.	Mean	S.D.
No CAD	29	0.0	50.0	6.30	12.09
CAD	13	0.0	200.0	94.69	74.85
Total	42	0.0	200.0	33.66	58.74

‘t’=6.271; *p*<0.001

Total calcium score of CAD patients (94.69±74.85; range: 0-200) was found to be significantly higher than that of No CAD (6.30±12.09; range: 0-50.0).

Table 14: Correlation of Epicardial Fat volume with Total calcium score, CIMT and hs-CRP

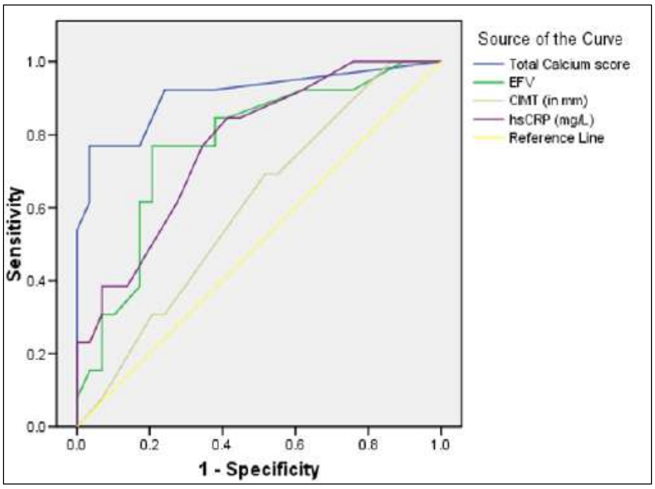
Variable	‘r’	Level	‘p’	Significance
Total calcium score	0.437	Mild	0.004	Highly significant
CIMT	0.243	Weak	0.121	Non-significant
hs-CRP	0.739	Strong	<0.001	Very highly significant

Epicardial fat volume (EFV) was found to be linearly correlated with Total Calcium score, CIMT and hs-CRP. Correlation of EFV and CIMT was found to be non-significant and Weak (r=0.243; p=0.121) while correlations of EFV with Total calcium score and hsCRP were found to be significant, level of correlation between EFV & Total calcium score was Mild and between EFV &hs-CRP was found to be strong.

Role of Total calcium score, EFV, CIMT and hsCRP for prediction of coronary artery disease had been shown in following Receiver-Operator Curve (ROC).

Table 15: Receiver-Operator Curve Analysis for detection of coronary artery disease using different predictors

Parameter	Area under curve	S.E.	‘p’	95% CI	
				Lower bound	Upper bound
Total Calcium score	0.908	0.057	<0.001	0.796	1.021
EFV	0.773	0.079	0.005	0.619	0.927
hsCRP (mg/L)	0.764	0.075	0.007	0.616	0.912
CIMT (in mm)	0.602	0.091	0.295	0.424	0.780



Graph 15: Receiver-Operator Curve using different predictors

	Derived cut-off	Sens. (%)	Spec. (%)	PPV (%)	NPV (%)	Diag. accuracy(%)
Total Ca Score	≥24.00	76.9	89.7	76.9	89.7	85.7
EFV	≥10.50 cc	76.9	79.3	62.5	88.5	78.6
hsCRP	≥3.30 mg/L	76.9	65.5	50.0	86.4	69.0

For prediction of Coronary artery disease, total calcium score, EFV, CIMT and hsCRP levels were evaluated. Area under curve for Total calcium score, EFV, CIMT and hsCRP were 0.908, 0.773, 0.602 and 0.765 respectively. CIMT was not found to be a significant predictor hence its cut-off value was not explored. Cut-off values for prediction of coronary artery disease were Total Calcium score ≥24.00, EFV ≥10.50 cc, and hsCRP ≥3.30 mg/L.

Sensitivity, Specificity, PPV, NPV of above predictors is shown in above table. Diagnostic accuracy of Total calcium score (85.7%) and EFV (78.6%) were satisfactory.

Discussion

With the economic progress and changes in lifestyle, a phenomenal change in health and disease status has become evident. Excepting the pandemic COVID-19 in the last one year, the major cause of death has shifted from infectious diseases to lifestyle diseases [10]. Over the last two decades, cardiovascular disease remains to rank first as the cause of death. Overall it is responsible for 31% of total deaths worldwide and the trends indicate it to remain unchanged upto the year 2030. Coronary artery disease (CAD) is one of the most common cardiovascular diseases with atherosclerosis being the underlying pathophysiology. With the atherosclerosis being the characteristic feature of CAD, an assessment of extent of atherosclerosis provides a measure of CAD and its progression [11]. Traditionally, arterial stenosis caused by atherosclerosis could be measured with the help of conventional angiography. In view of high accuracy of conventional coronary angiography (CCA), it is recognized as the gold standard for diagnosis of CAD. However, conventional angiography being an invasive procedure is carried out in highly suspicious patients and as such its role in screening and early evaluation of coronary artery disease is highly impractical [12].

In the recent years, with the emergence of various imaging modalities to visualize the atherosclerosis, recognition of some surrogate markers like C-reactive protein, other subclinical markers like carotid intima media thickness, a lot of hope has generated to assess the coronary artery disease and its progression through non-invasive measures and to carry out these studies for screening purposes too [13].

Though, the process of atherosclerosis is not fully understood yet it is believed that the mechanism of atherosclerosis basically involves lipid accumulation and immune activation in the vascular wall which is mediated by a host of other factors, including a number of specialized proteins and lipids, which are instrumental in stimulating inflammation and atherosclerosis. Epicardial fat is a fatty tissue found between the myocardium and the visceral pericardium. Primarily its function is to raise an immune barrier and to offer myocardial and coronary artery protection [14]. It is the local fatty acid source for the myocardium. However, when in excess it becomes hypoxic and dysfunctional. As a result there is increased lipolysis and consequent inflammation that leads to a shift in its metabolic profile altering the homeostasis. Through these changes, it has been shown to propagate the process of coronary atherosclerosis and plaque deposition leading to coronary artery disease [15].

With this background, the present study was carried out with an aim to evaluate epicardial fat volume by dual energy CT and its correlation with coronary artery calcium scoring, CIMT, High sensitivity –CRP in coronary artery disease. For this purpose, a total of 42 patients clinically suspected of coronary artery disease were enrolled in the study and underwent clinic-radiological and biochemical evaluation.

Recommendations of the study: Although CT angio/ angiography are the gold standard for diagnosis of CAD, however, EFV by DECT is novel, noninvasive, nearly comparable method for assessment of CVR and combination of EFV, hsCRP and Total calcium score are all reliable, non-invasive markers for assessment of CVR. However further studies are recommended with larger sample size to evaluate CIMT as a noninvasive marker for the assessment of CVR.

Conclusion

A total of 42 patients presenting with chest pain at Department of Cardiology were enrolled. Of these 42 patients, 13 (31.0%) were confirmed to be suffering from Coronary artery disease and rest 29 (69.0%) confirmed as not suffering from Coronary artery. CAD patients were older and higher BMI than No CAD patients. Gender did not show any significant association with CAD. Correlation of EFV with Total Calcium score and hs-CRP were significant. Correlation of EFV and CIMT was not found to be significant. Total Calcium score, EFV and hsCRP were found to be significant predictors of coronary artery disease (Area under curve 0.908, 0.773 and 0.764 respectively).

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