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RESEARCH ARTICLE

VALUE OF EPICARDIAL ADIPOSE TISSUE ASSESSMENT BY CARDIAC COMPUTERIZED TOMOGRAPHY IN HEART FAILURE PATIENTS WITH PRESERVED EJECTION FRACTION

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Abstract

Objectives: A major problem that increases the morbidity and mortality is Heart failure with preserved ejection fraction (HFpEF)in comparison toheart failure with reduced ejection fraction (HFrEF). Adipose tissue and the linked inflammation were shown to contribute in HF pathogenesis and constitute a unique phenotype of HF. HFpEF patients tend to be obese. So, we aimed to assess the epicardial adipocytes (EAT) noninvasively by measuring the volume of EATthroughComputerizedtomography (CT) among HFpEFpatients and correlates it with echocardiographic diastolic dysfunction measures.
Study design: We enrolled 76 participants divided into two groups: 38 patients with HFpEF with LVEF > 50% on echocardiography and 38 controls at outpatient clinic and a radiology department at National Heart Institute. All included participants had noninvasive assessment of the epicardial adipose tissue volume using cardiac CT.
Results: Regarding Baseline Demographic characteristics, mean age (SD) of participants:57.45 (6.0) with high prevalence of risk factors (DM, Dyslipidemia, smoking) among HFpEF patients with no significant difference statistically among groups. Also, asiginificant difference statistically was found amongthe enrolled groups regarding echocardiographic findings (LVEF%, Mean E/e`ratio, est. LVEDP and Tricuspid Regurge V). The epicardial fat Volume was significantly high at HFpEF group (P < 0.001).
Conclusions: We found that high grade diastolic dysfunction was associated with epicardial fat that appeared to be greater in HFpEF patients. As a result, we found that epicardial fat could be used as a different marker for both HFpEF and diastolic dysfunction.

Introduction:-

There is an increasingly health concern about morbidity and moratlity rate of HFpEF, where the LV ejection fraction is greater than 40%, in comparison to HFrEF.

No specific medications to reduce morbidity and mortality despite increasing incidence of HFpEF till now; this may be attributed to the disease's heterogeneity [1].

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HFpEF is a multifactorial illness with numerous pathways with variety of clinical symptoms, it has been challenging to develop a limited set of inclusion criteria for clinical studies [2]. Adipose tissue and the linked inflammation were shown to contribute in HF pathogenesis of HFpEF, which is supported by the fact that many individuals with HFpEF are obese. Additionally, it seems to represent a unique phenotype on the HF continuum [3].

Adipose tissue known as EAT is placed between myocardium and pericardium's visceral layer. This tissue is distinguished by extremely active thermogenic genes and fatty acid production [4]. Pluripotent cells and cytokines can move in both directions due to the unhindered microcirculation that exists between the epicardium and surrounding cardiac tissues. Healthy EATmake a protein called adiponectin that shields cardiomyocytes from hypertrophic stimuli and reduces cardiac fibrosis. Despite acting like an inducer for systemic inflammatory responses that might alter underlying cardiac and vascular composition, systemic inflammation, on the other hand, causes a radical change in the biological and physiological characteristics of the epicardium, enabling it to abandon its nutritive role and develop pro-inflammatory properties [5].

Using CT, thickness or volume of EAT may be measured non-invasively or magnetic resonance imaging due to epicardial adipocyte aberrant proliferation. The transformation of the epicardium has the potential to harm the ventricular myocardium, causing fibrosis in the heart, diminished ventricular dispensability, and reduction in the density of microvasculature, which are all pathological findings of HFpEF[6].

Aim of Work

We aimed to assess epicardial adipocytes noninvasively by measuring EAT volume using CT amongHfpEFpeople and associate it with echo diastolic dysfunction parameters.

Study Design:

This was acase-control, researchwhich included76 participants divided into two groups: 38 cases and 38 controls at outpatient clinic and a radiology department at National Heart Institute with Inclusion criteriaas following:

1. Subjects who hadHF symptoms (New York Heart Association functional class ≥II) who have a LVEF >50% on echo.
2. LVD dysfunction (LVDD), left atrial dilatation (LAD) and/or left ventricular hypertrophy (LVH) by transthoracic echocardiographic assessment.

Exclusion criteria:

1. Patients with LVEF ≤ 40% on echocardiography.
2. Subjects who had congenital anomalies in the heart.
3. Subjectswith> moderate valvular disease in the left side.

Participants were subjected to the following:

1. Complete History with emphasis on age, gender, occupation.
2. Medical History: Assessment of HF symptoms, risk factors (hypertension, DM, dyslipidemia and smoking).
3. Family History.
4. Clinical Examination: General examination, chest examination and local examination.
5. Serum creatinine was done for all participants.
6. Transthoracic echocardiography: echocardiography was used to all patients:
7. left ventricular ejection fraction (LVEF) was checked by M-Mode and Simpsons technique.
8. Diastolic parameters were assessed by tissue Doppler, Doppler flow.
9. Left atrium morphology and biplane LA volume were assessed by using area length method [7].

Computerized Tomography (CT):

1. EFV was measured using a dual source 64-slice CT scanner.
2. Parietal pericardium was manually traced in every fourth slice from aortic root to cardiac apex using 3.0-mm thick axial slices utilized to score calcium.
3. Software then inserted and tracked parietal pericardium in slices in between hand drawn slices.
4. Automatically traced slices' Accuracy was checked.
5. Threshold attenuation ranges from -30 to -190 HU Fat voxels were revealed.

Ethical considerations:

1. Patients were informed about study steps with its possible complications focusing on the importance of data they were going to offer.
2. Patients who participated in this study provided written informed consent, indicating that they had received complete information regarding the procedures and potential hazards.
3. No one who was not a direct participant in the study was given access to any participant data or study outcomes since they were confidential.
4. Any abnormal test and procedure results were shared with the patients.
5. The patients had freedom to decline participation without jeopardizing medical treatment that is anticipated to be provided to patients

Statistical Analysis:

Gathered data were processed with SPSS version 23.0. When distribution was parametric, quantitative data were given as mean, SD &ranges. Non-parametric variables were presented in median with IQR. Qualitative factors were also given numerically and as percentages. Kolmogorov-Smirnov and Shapiro-Wilk tests were used for normality testing. Independent-samples t-test was used to compare means. For two-group comparisons among non-parametric variables, Mann Whitney U test was utilized, and the Chi-square test of significance was utilized for proportionscomparing among qualitative parameters. CI was 95%, while acceptable margin of error was 5%. P-value was deemed significant as follows: P-values less than 0.05: significant, P-values greater than 0.00: highly significant, and P-values greater than 0.05: insignificant.

Results:-

Table 1:- Demographic and clinical data of HFpEF and control groups:

Variables	HFpEF N = 38	Control N = 38	Test value	P value
	N (%) / Mean ± SD			
Age (Years)	58.4 ± 6.3	56.5 ± 5.7	t:1.379	0.172
Sex Male Female	 33 (86.8) 5 (13.2)	 30 (78.9) 8 (21.1)	x^2:0.371	0.542
HTN	17 (44.7)	22 (57.9)	x^2:1.308	0.253
DM	23 (60.5)	21 (55.3)	x^2:0.208	0.648
Dyslipidemia	21 (55.3)	18 (47.4)	x^2:0.468	0.494
Smoking	19 (50)	17 (44.7)	x^2:0.211	0.646
BMI	27.3 ± 1.5	26.8 ± 1.7	t:1.360	0.178
Serum Cr	1.06 ± 0.2	1.03 ± 0.1	t:0.827	0.411

HTN: hypertension, DM: Diabetes mellitus, BMI: body mass index,
Using: t-Independent Sample t-test; x^2: Chi-square test
p-value >0.05 is insignificant

Table 2:- Echocardiography Doppler Findings of both groups:

Variables	HFpEF N = 38	Control N = 38	Test value	P value
	Mean ± SD / Median (Min – Max)			
EF (%)	59.5 ± 5.9	62.9 ± 4.8	t:2.756	0.007*
LVESD (mm)	37.6 ± 6.4	35.3 ± 6.2	t:1.591	0.116
LVEDD (mm)	51.9 ± 8.6	52.9 ± 7.9	t:0.528	0.599
ESV (ml)	53 (23-139)	51(12-106)	U:1.291	0.291
EDV (ml)	139.7 ± 49.1	135 ± 45.6	t:0.432	0.667
LVMI (gm/m2)	104.9 ± 28.7	101.2 ± 25.6	t:0.593	0.555
LVH N (%)	13 (34.2)	8 (21.1)	x^2:1.608	0.205
RWT (Relative Wall Thickness)	0.375 ± 0.09	0.339 ± 0.08	t:1.843	0.069
LA Diameter (mm)	36.7 ± 9.8	38.1 ± 4.2	t:0.809	0.421
E/A ratio	0.9 (0.5-3.7)	0.8 (0.5-2.1)	U:0.619	0.728
DT (ms)	201.5 ± 63.9	217.8 ± 46.7	t:1.270	0.208

IVRT(ms)	116.7 ± 34.9	113.6 ± 24.5	t:0.448	0.655
Septal e´(cm/s)	0.08 ± 0.03	0.09 ± 0.01	t:1.949	0.055
lateral e`(cm/s)	0.09 (0.05-0.9)	0.1 (0.09-0.2)	U:0.551	0.167
Mean E/e`ratio	10.8 ± 3.1	6.2 ± 1.7	t:8.020	<0.001**
DD grade N (%) Grade I Grade II Grade III	20 (52.6) 11 (28.9) 7 (18.4)	NA	--	--
est. LVEDP (mmHg)	13.9 ± 3.1	10.1 ± 1.6	t:6.715	<0.001**
LAVI (mL/m2)	34 (17-81)	36 (17-75)	U:1.071	0.681
Tricuspid Regurge V (M/s)	2.5 (0-4.1)	0 (0-3)	U:4.195	<0.001**

Using: t-Independent Sample t-test; U: Mann-Whitney test; x^2: Chi-square test
p-value >0.05 is insignificant; *p-value <0.05 is significant; **p-value <0.001 is highly significant

Table 3:- CT Parameters of both groups:

Variables	**HFpEF N = 38**	**Control N = 38**	**Test value**	**P value**
	N (%) / Mean ± SD			
Epicardial fat Volume (cm3)	148.1 ± 27.6	97.3 ± 19.8	9.219	<0.001**
Epicardial fat Height (Cm)	7.3 ± 0.9	6.9 ± 0.4	2.504	0.015*
Epicardial fat Mean (Hu)	-41.2 ± 12.9	-40.9 ± 15.3	0.092	0.927

Using: t-Independent Sample t-test
p-value >0.05 is insignificant; *p-value <0.05 is significant; **p-value <0.001 is highly significant

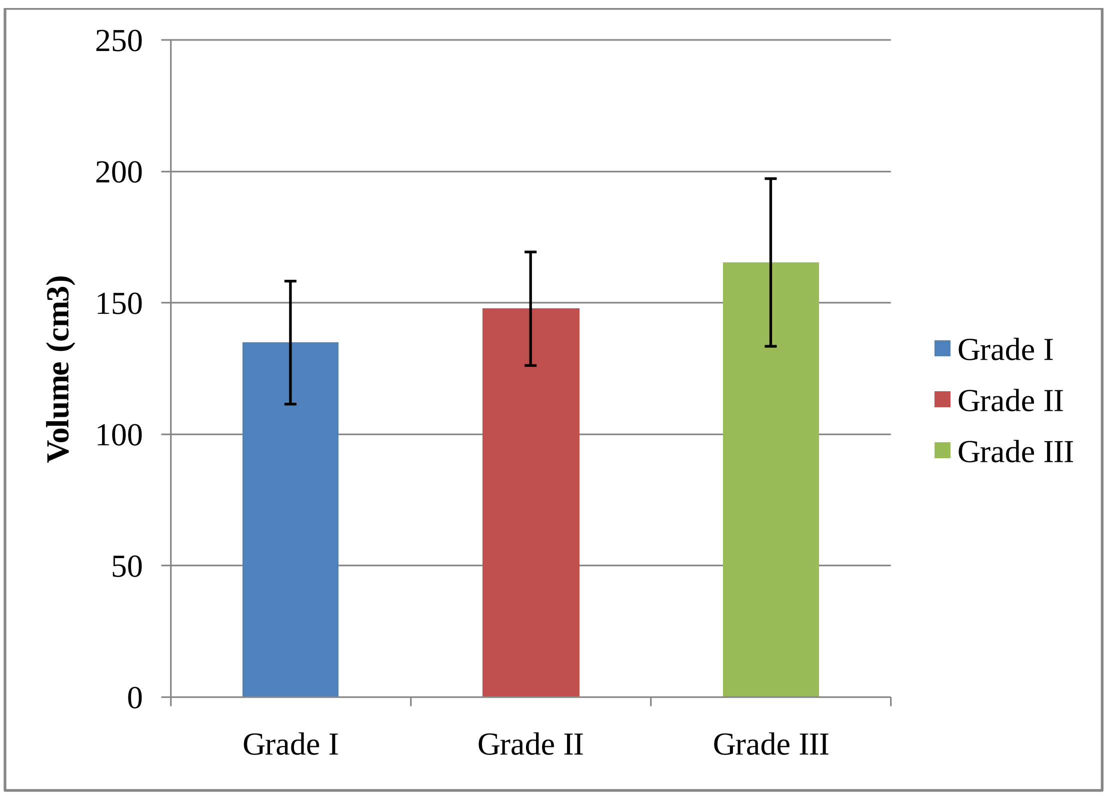

Figure 1:- Comparison of diastolic dysfunction grade according to epicardial fat volume in HFpEF group.

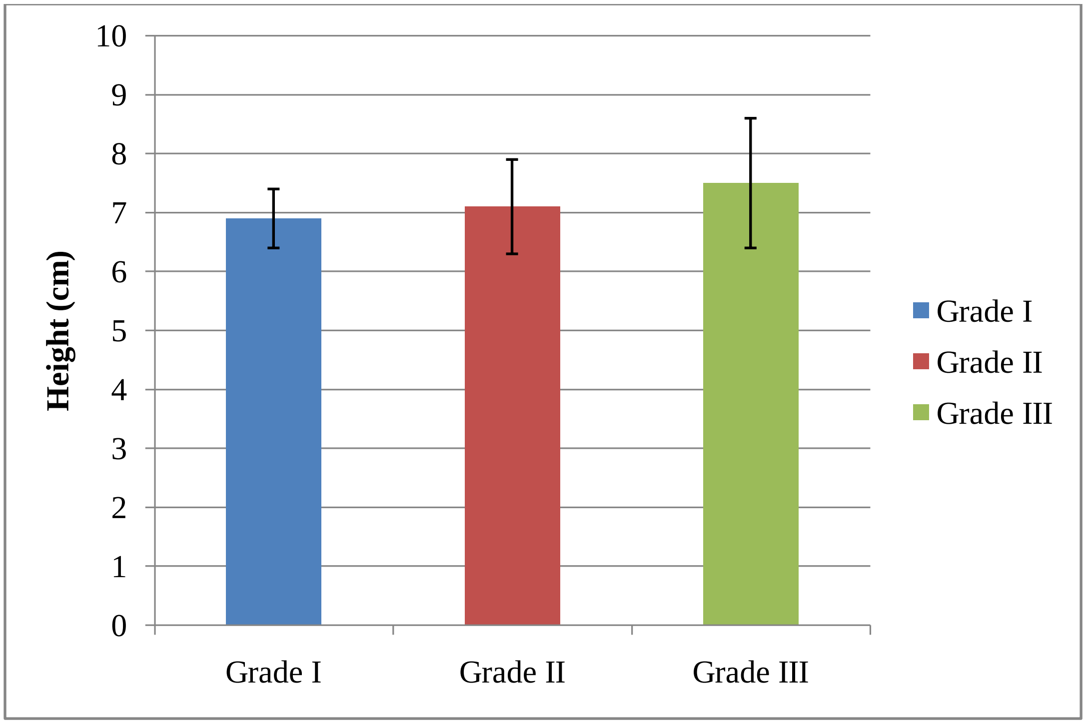

Figure 2:- Comparison of diastolic dysfunction grade according to epicardial fat height in HFpEF group.

Discussion:-

In our study we used cardiac CT to assess EAT in patients with HFpEF in comparison with healthy people with similar BMI.

We found no statistically significant differencewaspresentamongHFpEF and controls regarding demographic & clinical data (age, sex, HTN, DM, smoking, BMI, and serum Creatinine) ($P>0.05$). the socioeconomic histories of both groups were similar with little impact on the study's overall findings.

According to CT parameters, the HFpEF group had a statistically significant increase in epicardial fat volume and epicardial fat height($P<0.001$) relative to the control groups (148.1 ± 27.6 vs 97.3 ± 19.8), (7.3 ± 0.9 vs 6.9 ± 0.4), and no statistically significant differenceamong EAT mean ($P>0.05$) between the two groups. This finding is consistent with that of **Van Woerden et al. (2018)**, who conducted a study of 64 HFpEF and mid-range ejection fraction (HFmrEF) patients & 34 healthy people [(8)]. **Doesch et al. (2010),** on the other hand, conducted a study of 66 patients with CHF, caused by, ischemic or dilated cardiomyopathy and 32 stable controls. They found that CHF patients had lower EAT mass than controls (22 ± 5 g/m2Vs 34 ± 4 g/m2, $p <0.0001$). Difference between these outcomes may be due to that the level of epicardial fat in HFpEF patients with advanced BMI and age was smaller than among stable HFpEFcontrols [(9)]**.**

We compared diastolic dysfunction grade to epicardial fat (volume, height and mean) inHFpEF group, no statistically significant differences were found in epicardial fat parameters height and mean ($p>0.05$), but there was significant increase in epicardial fat volume ($P<0.05$) between grade I and grade III. This statement was further supported by [(8)].

Our study found statistically significant differencesregarding epicardial fat volume, epicardial fat height, LVEF%, and mean E/e`ratio in HFpEF group ($P<0.05$), but no significant correlations among remaining variables ($P>0.05$). Furthermore, the importance of epicardial fat assessment as an indicator for HFpEF, with high sensitivity and accuracy.

Conclusion:-

The current study showed that high grade of diastolic dysfunction was associated with epicardial fat that appeared to be greater in HFpEF patients. As a result, we found that epicardial fat could be used as a different marker for both HFpEF and diastolic dysfunction.

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