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Original article

Improved Subclinical Left Ventricular Dysfunction by Global Longitudinal Strain in Dyslipidemic Patients After Statin Therapy

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Abstract

Background: Dyslipidemia is still a significant cardiovascular disease risk factor. The mainstay of care for patients with dyslipidemia is statin medication. Slight alterations in the left ventricle's functionality can be detected with an imaging method called global longitudinal systolic strain (GLSS) (LV). **Aim:** to evaluate the pre- and post-statin therapy subclinical structural cardiac changes in dyslipidemic individuals. **Patients and methods:** Thirty dyslipidemic patients and thirty matched controls underwent testing for lipid profile, conventional echocardiography, and 2D speckle tracking. Dyslipidemic patients received statin and followed up after 6 months of therapy with re-evaluation for lipid profile, conventional echocardiography, and 2D speckle tracking. **Results:** GLSS was impaired in dyslipidemic patients in comparison with controls. This impairment was improved after 6 months of statin therapy. The global longitudinal strain values were -18.12 (-24.29: -10.71) before statin, and -20.5 (-24.35: -13.35) following statin ($p < 0.001$). **Conclusion:** Patients with dyslipidemia may have normal systolic function as determined by the EF technique, but they also have impaired global and segmental longitudinal systolic strain. This indicates the existence of subclinical left ventricular systolic dysfunction, which is improved by statins.

Keywords: Dyslipidemia, Statin therapy, Strain imaging.

Introduction

Dyslipidemia continues to be a fundamental risk factor for cardiovascular disorders, which are responsible for one-third of all global deaths [1]. Dyslipidemia refers to an abnormal increase in the levels of lipids in the bloodstream, specifically cholesterol (TC), triglyceride (TG), and low-density lipoprotein (LDL), together with a decrease in high-density lipoprotein (HDL). Dyslipidemia may exert a contrasting impact on the left ventricle (LV) function [2].

Administering statin medication can substantially decrease the risk of cardiovascular death in adults with dyslipidemia. Statin medication is the principal treatment for preventing cardiovascular ischemic events in patients with dyslipidemia, both for those who have not had a previous incident (primary prevention) and for those who have established cardiovascular disease (secondary prevention) [3].

Statins have plentiful pleiotropic effects, such as decreasing platelet activation, coagulation, and endothelin levels while increasing endothelial function, nitric oxide bioavailability, and endothelial progenitor cells. They also decrease reactive oxygen species, and immunomodulation [4]. The aforementioned advantageous characteristics are all cellular or molecular in nature; nevertheless, there is insufficient data about structural heart alterations in patients receiving statin therapy.

Global longitudinal systolic strain (GLSS) is a precise and reliable imaging technique used to measure subtle abnormalities in the LV. GLSS, or global longitudinal strain, can identify the contraction of the innermost layer of the heart muscle. This contraction is often observed before a noticeable decrease in the left ventricle's ejection.fraction. (EF) [5].

Aim:

We aimed to evaluate the pre- and post-statin therapy subclinical structural cardiac changes in dyslipidemic individuals.

Methodology:

Study type: Case-control study with prospective case follow-up.

Study location:

The study was carried out at Mansoura University Hospitals' Department of Cardiovascular Medicine.

Study duration:

The study was carried out between January 2020 and December 2022. The study was interrupted during this period of COVID 19 pandemic due to strict hospital rules and patients’ refusal to participate in studies.

Sample size:

Using IBM¨ SPSS¨ Sample Power¨ version 3.0.1 (IBMª Corp., Armonk, NY, USA), the necessary sample size was determined based on a thorough evaluation of a study by Morimoto et al. [6] evaluating LV function prior to and six months following statin use. With a power of 90% and a significance threshold of 95%, 26 cases were the bare minimum sample size needed. The sample size needed to account for dropouts was raised to thirty cases.

Study population:

Before starting statin therapy, we studied thirty dyslipidemic patients (study group)

aged from 40 to 59 years and thirty healthy participants (control group) who were the same age and sex and did not have any cardiovascular risk factors or obesity. Following statin medication, we monitored patients with dyslipidemia for six months.

Inclusion criteria:

Adult dyslipidemic individuals without previous history of CVD and met the following inclusion criteria:

The American Heart Association's criteria, which state that a person has dyslipidemia if their total cholesterol is above 5.2 mmol/L (200 mg/dl), their LDL is above 3.4 mmol/L (130 mg/dl), their HDL is below 0.9 mmol/L (35 mg/dl), their triglyceride is above 1.7 mmol/L (150 mg/dl), or a combination of these variables [7]. Before beginning statin therapy, these criteria were used, and patients underwent six months of follow-up care.

Exclusion criteria:

Exclusion criteria for the study included patients with congenital or valvular heart diseases, cardiomyopathy, arrhythmia, hypertension, diabetes mellitus, known coronary heart diseases, typical chest pain, ECG suggestive of myocardial ischemia thyroid disorders and liver or kidney dysfunction.

Demographic and clinical data:

Information was obtained about the age, sex, height, weight, body mass index (BMI), history of type 2 diabetes mellitus (T2DM), smoking habits, obesity status, systolic and diastolic blood pressure (SBP and DBP), and pharmaceutical therapy of the subjects.

Laboratory investigations

Pre- and post-six-month follow-up laboratory tests were conducted, including total serum cholesterol, triglycerides, LDL-C, HDL-C, ALT, AST, TSH and HbA1C.

Electrocardiography:

A twelve-lead ECG was done for all participants. All participants had a normal ECG without ST-T wave change or arrhythmias.

Echocardiography

A routine echocardiography by a commercially available ultrasound-machine (Vivid E9, GE Vingmed Ultrasound AS in Horten, Norway) was used for scanning and processing.

The active matrix single-crystal phased-array transducer, GE M5S-D, was employed (GE Vingmed Ultrasound AS). We improved the quality of grayscale recordings by attaining an average frame rate of 50 frames per second. Cardiac chamber measures were acquired using transthoracic echocardiography, adhering to established guidelines.

Two-dimensional imaging in the parasternal long axis, apical long axis, apical 2 chamber, and apical 4 chamber views were used to perform echocardiography. The left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), and left ventricular ejection percent (LV EF) were measured using the M mode.

Speckle-tracking echocardiography:

Vivid E9, GE Vingmed Ultrasound AS in Horten, Norway was used for scanning and processing.

For three to five consecutive cardiac cycles, high-resolution moving images of the apical

four-, two-, and three-chamber long axis views were captured. Subsequently, the speckles were meticulously traced on a frame-by-frame basis using Automated Function Imaging (AFI), a specialized software designed for speckle tracking. Areas of interest were recognized in the basal, mid, and apical areas. The operator manually corrected segments that were unable to be tracked. Three apical views were used to calculate the LV 2D longitudinal systolic strain to the strain value at aortic valve closure. It was measured with the Bull's Eye in 17 segments. Longitudinal systolic deformation is defined as the process of becoming shorter, and systolic indices are represented by negative numbers. The strain values of all 17 segments were averaged to determine the global longitudinal systolic strain. Prior research has shown that persons in good health exhibit global longitudinal strain (GLS) values ranging from -16% to -19%. A threshold of -16% is considered impaired GLS [8]. Post processing was performed

Statin therapy:

We utilized high and moderate statin medication according to guidelines recommendations and SCORE risk score [9].

Ethical consideration (consent):

The study was approved by Mansoura University's Medical Ethics Committee and Institutional Research Board (IRB) under reference number MD.19.04.170. Each patient who was part of the study gave his/her informed consent to have an echocardiogram as well as to participate in the trial.

Statistical Analysis

The analysis of the collected data was done with SPSS version 26 (New York, USA by IBM 2019**)**. First, we performed a one-sample Shapiro-Wilk test to see whether the data were normal. By giving qualitative data numerical values and expressing them as percentages, we transformed them into quantitative forms. For normally distributed data, continuous variables were shown as the mean ± SD; for non-normally distributed data, they were shown as the median, minimum, and maximum. For normally distributed data, a paired t-test was employed to compare the variables before and after statin medication; for non-normally distributed data, a Wilcoxon signed rank test was utilized. Categorical data was evaluated using the McNemar test. The statistical analysis was carried out utilizing (SPSS Inc. software from Chicago, Illinois, USA). The groups were compared using the Mann Whitney test for data that did not meet the assumptions of parametric testing, the Chi-square test or Fisher's exact test for categorical data, and the independent samples t-test for data that had a normal distribution. A statistical significance threshold of $P < 0.05$ was employed to ascertain the significance.

Results:

Regarding demographic parameters, dyslipidemic patients and control were age, sex, and risk factors matched ($p > 0.05$), with higher body mass index in dyslipidemic patients ($P <0.001$). Total cholesterol, LDL and triglycerides were statistically significant higher in dyslipidemic patients ($P <0.001$). Echocardiography left ventricular

dimensions, ejection fraction and fraction shortening were non-statistically significant different in dyslipidemic patients and control, while global longitudinal strain was statistically significant impaired in dyslipidemic patients (**Table 1**).

In comparing dyslipidemic patients pre and post statin; total cholesterol, LDL and triglycerides were statistically significant lower after six months of statin therapy (p value <0.001, <0.001, and 0.009 respectively) (**Table 2**).

Left ventricular dimensions and function was non statistically significant different after six months of statin therapy (p value > 0.05), while global longitudinal strain and multiple segmental longitudinal strain were statistically significant different after six months of statin therapy; indicating improving of longitudinal strain with therapy **(Table 3**).

When comparing dyslipidemic patients after 6 months of statin and control; there were non-statistically significant difference in demographic parameters, laboratory, and echocardiographic findings (P > 0.05) except BMI still statistically significant higher in dyslipidemic patients (P <0.001) (**Table 4**).

Table (1): Demographic parameters, laboratory, and echocardiographic findings of control and dyslipidemic patients pre-statin.

Parameter		Dyslipidemic Pre- statin (30)	Control (30)		P value
Demographic parameters					
Age (year)		49 ±9.1	45.9 ±4.7	t= 1.2	0.15
Sex	**Male**	17 (٥٦.7%)	7 (46.7%)	χ2=0.٤	0.٧5
	Female	13 (43.3%)	8 (53.3%)		
Height (meter)		1.7 ±0.05	1.7 ± 0.9	t= -0.84	0.41
Weight (Kg)		93.3 ±10.5	79.1 ± 11.9	t= 4.1	**<0.001***
BMI (kg/m^2)		32.3 ± 3.1	26.6 ± 2.0	t= 6.5	**<0.001***
Smoking	**Yes**	7(23.3%)	2(13.3%)	FET	0.7
	No	23(76.7%)	13(86.7%)		
Diabetes	**Yes**	0	0		
	No	30(100%)	15(100%)		
Blood pressure	**SBP**	120 (110-135)	120 (110-130)	Z=-0.5	0.6
mmHg	**DBP**	80 (70 - 85)	80 (70- 85)	Z=-0.2	0.8
Laboratory findings					
Total Cholesterol (mg/dL)		265.6 ± 36.8	180.6 ± 11.8	t= 8.7	**<0.001***
LDL (mg/dL)		157.0 (119.0 - 258.0)	112.9 (86.0 - 128.0)	Z=-5.1	**<0.001***
HDL (mg/dL)		46.5 (6.0 - 70.0)	52.0 (34.0- 63.0)	Z=-1.0	0.3
Triglycerides (mg/dL)		166 (73.0- 788.0)	96.5 (40.0-139.0)	Z=-3.6	**<0.001***
TSH (µIU/mL)		1.8 (0.9- 4.1)	1.4 (0.1- 4.1)	Z=-1.2	0.2
RBS (mg/dL)		109 (76- 187)	117 (86- 178)	Z=-0.3	0.8
HbA1C (%)		4.6 ± 0.6	4.8 ± 0.4	t=-0.8	0.4
ALT (U/L)		31 (19-44)	18.8 (14- 33)	Z=-4.2	**<0.001***
AST (U/L)		30.6 ± 7.2	22.6 ±9.2	t=3.1	**0.003***
Echocardiographic findings					
LVEDD (mm)		4.8 ± 0.3	4.6 ± 0.5	t= 1.7	0.1
LVESD (mm)		3.0 ± 0.3	2.8 ± 0.3	t= 1.6	0.1
EF (%)		66.6 ± 5.9	68.0 ± 3.6	t= - 0.8	0.4
FS (%)		36 (29-52)	37 (33-45)	Z= -0.7	0.5
GLS (%)		-17.9 ± 3.3	-20.2 ± 1.5	t = 2.5	**0.015***

Abbreviations: Aspartate transaminase (AST) and alanine transaminase (ALT) Body Mass Index (BMI) Diastolic blood pressure (DBP), fraction shortening (FS), and ejection fraction (EF), Hemoglobin A1C (HbA1C), or global longitudinal strain (GLS), High-density lipoprotein cholesterol (HDL), Low-density lipoprotein cholesterol (LDL), Left ventricular end-diastolic dimensions (LVEDD), Left ventricular end-systolic dimensions ((LVESD), Meter (M), Random blood sugar ((RBS), Systolic blood pressure (SBP), Thyroid stimulating hormone (TSH).
T= independent t test, Z: Mann Whitney test, χ2= Chi square test FET= Fisher's Exact Test, *p value <0.05: significant

Table (2): Dyslipidemic patients' demographic parameters, and laboratory findings pre and post statin**.**

Parameter	Pre- Statin (30)	Post- Statin (30)	t	P value
Demographic parameters				
Height (m)	**1.69 ± 0.05**	**1.69 ± 0.05**	**0.30**	0.76
Weight (Kg)	**93.30 ± 10.51**	**88.73 ± 14.69**	**2.66**	0.012
BMI (kg/m^2)	**32.33 ± 3.08**	**30.74 ± 4.58**	**2.91**	**0.007***
Smoking				
Yes	**7 (23.33%)**	**1 (3.3%)**		0.03
No	**23 (76.67%)**	**29 (96.7%)**		
Diabetes mellitus				
Yes	**0 (0%)**	**4 (13.3%)**		
No	**30 (100%)**	**26 (86.7%)**		0.125
Blood pressure				
SBP	**120 (110-135)**	**120 (110-160)**	**0.74**	0.46
DBP	**80 (70-85)**	**80 (70-100)**	**0.1**	0.68
Laboratory findings				
Total Cholesterol (mg/dL)	**265.63 ± 36.75 mg/dL**	**197.80 ± 48.85 mg/dL**	**t= 6.63**	**< 0.001***
LDL (mg/dL)	**157.0 (119-258) mg/dL**	**100.5 (38-265) mg/dL**	**Z= -3.56**	**< 0.001***
HDL (mg/dL)	**46. 0 (6-70) mg/dL**	**49.5 (14-68) mg/dL**	**Z= -0.606**	0.545
Triglycerides (mg/dL)	**166 (73-788) mg/dL**	**110.5 (57-318) mg/dL**	**Z= -2.63**	**0.009***
TSH (µIU/mL)	**1.8 (0.9-4.1)**	**1.8 (0.9-4.0)**	**Z= -1.45**	0.15
RBS (mg/dL)	**109 (76-187)**	**124 (84-320)**	**Z= -2.34**	0.02
HbA1C (%)	**4.5 (3.8-5.8)**	**4.5 (3.9-9.2)**	**Z= -0.96**	0.34
ALT (U/L)	**28.5 (19-44)**	**28.5 (7-76)**	**Z= -0.24**	0.81
AST (U/L)	**31.5 (18-43)**	**25.5 (11-66)**	**Z= -0.72**	0.47

Abbreviations: as in Table 1.

McNemar test, T: Paired-t test, Z: Wilcoxon-Signed-Ranks test *p value <0.05: significant.

Table (3): Dyslipidemic patients' echocardiographic measures pre and post statin.

Parameter	Pre- Statin (30)	Post- Statin (30)		P value
Conventional echocardiographic measures				
LVEDD (mm)	4.79 ± 0.32	4.74 ± 0.34	t=0.75	0.46
LVESD (mm)	2.98 ± 0.34	2.98 ± 0.29	t=0.05	0.96
EF (%)	66.63 ± 5.89	67.03 ± 4.60	t=-0.31	0.76
FS	37.03 ± 4.74	37.10 ± 3.71	t=-0.06	0.95
Global and segmental longitudinal strain measures				
GLS	-18.12 (-24.29: -10.71)	-20.5 (-24.35: -13.35)	Z= -4.60	< 0.001*
Apex	-23.10 ± 7.11	-26.17 ± 5.23	t= 3.20	0.003*
Apical Septal	-23.00 ± 5.75	-24.83 ± 3.75	t= 2.19	0.04*
Apical Anterior	-21.90 ± 6.50	-21.93 ± 5.19	t= 0.03	0.98
Apical Lateral	-21.07 ± 7.32	-23.10 ± 5.89	t= 1.71	0.1
Apical Inferior	-21.40 ± 6.32	-22.80 ± 4.40	t= 1.47	0.15
Mid anteroseptal	-20 (-31: -13)	-22 (-28: -10)	Z= - 2.59	0.001*
Mid anterior	-18.5 (-25: -2)	-20 (-27: 0)	Z= -2.53	0.01*
Mid anterolateral	-17.53 ± 4.99	-20.90 ± 3.44	t= 3.57	0.001*
Mid inferolateral	-18 (-23: -8)	-18 (-24: -22)	Z= -1.75	0.08
Mid inferior	-18.5 (-26: -4)	-20 (-27: -10)	Z= -2.30	0.02*
Mid inferoseptal	-17.63 ± 5.08	-20.13 ± 4.21	t= 3.06	0.005*
Basal anteroseptal	-14 (-26: -6)	-18 (-23: -5)	Z= -3.25	0.001*
Basal anterior	-16 (-24: -5)	-18 (-23: -3)	Z= -1.73	0.08
Basal anterolateral	-14 (-23: -5)	-20 (-26: -10)	Z= -4.13	< 0.001*
Basal inferolateral	-14 (-23: -3)	-18 (-23: -7)	Z= -2.23	0.03*
Basal inferior	-16 (-26: -6)	-18 (-28: -6)	Z= -3.26	0.001*
Basal inferoseptal	-13 (-24: -7)	-17 (-22: -10)	Z= -3.64	< 0.001*

Abbreviations: as in Table 1

T: Paired-t test, Z: Wilcoxon-Signed-Ranks test, *: significant at p < 0.05

Table (4): Demographic parameters, laboratory, and echocardiographic findings of control and dyslipidemic patients post-statin.

Parameter		Dyslipidemic patients Post-statin (30)	Control (30)		P value
Demographic parameters					
Age (year)		**49 ±9.2**	**45.9 ±4.7**	**t= 1.2**	0.15
Sex	**Male**	**17 (56.67%)**	**7(46.7%)**	**χ2=0.٤**	0.٧5
	Female	**13 (43.33 %)**	**8(53.3%)**		
Height (meter)		**1.7 ±0.05**	**1.7 ± 0.9**	**t= -1.0**	0.3
Weight (Kg)		**87.5 (63-117)**	**84 (58-93)**	**Z=-1.7**	0.09
BMI (kg/m2)		**30.7± 4.6**	**26.6 ± 2.0**	**t=4.16**	**< 0.001***
Smoking	**Yes**	**1**	**2**	**FET**	0.25
	No	**29**	**13**		
Diabetes	**Yes**	**4 (13.3%)**	**0**	**FET**	0.28
	No	**26 (86.7%)**	**15**		
Blood pressure	**SBP**	**120 (110-160)**	**120 (110-130)**	**Z=-0.71**	0.48
	DBP	**80 (70- 100)**	**80 (70- 85)**	**Z= -0.30**	0.76
Laboratory findings					
Total Cholesterol (mg/dL)		**198.8 ± 48.9**	**180.6 ± 11.8**	**t= 1.83**	0.08
LDL (mg/dL)		**100.5 (38:265)**	**112.9 (86.0: 128.0)**	**Z=-0.28**	0.78
HDL (mg/dL)		**47.7 ± 12.4**	**49.7 ± 8.4**	**t=-0.56**	0.58
Triglycerides (mg/dL)		**110.5 (57-318)**	**96.5 (40.0-139.0)**	**Z=-1.36**	0.17
TSH (µIU/mL)		**1.8 (0.86-4)**	**1.4 (0.1- 4.1)**	**Z=-1.10**	0.27
RBS (mg/dL)		**140 (84- 320)**	**117 (86- 178)**	**Z=-0.63**	0.53
HBA1C (%)		**4.6 (3.9-9.2)**	**4.7 (4.1-5.5)**	**Z=-1.33**	0.18
ALT (U/L)		**28.5 (7-76)**	**18.8 (14- 33)**	**Z=-2.95**	0.003
AST (U/L)		**25.5 (11- 66)**	**21 (12.1-40)**	**Z= -1.33**	0.19
Echocardiographic findings					
LVEDD (mm)		**4.7 ± 0.3**	**4.6 ± 0.5**	**1.23**	0.23
LVESD (mm)		**3.0 ± 0.3**	**2.8 ± 0.3**	**1.69**	0.1
EF (%)		**67.0 ± 4.6**	**68.0 ± 3.6**	**- 0.71**	0.48
FS (%)		**37.1 ± 3.7**	**37.7 ± 3.1**	**-0.57**	0.57
GLS (%)		**-20.5 (-24: -13)**	**- 20 (-18: -23)**	**Z= -0.59**	0.55

Abbreviations: as in Table 1.

T= independent-t-test, Z: Mann-Whitney test, χ2= Chi-square test FET= Fisher's-Exact Test, *p value <0.05: significant

Figure 1 illustrates the improvement of GLS after statin therapy.

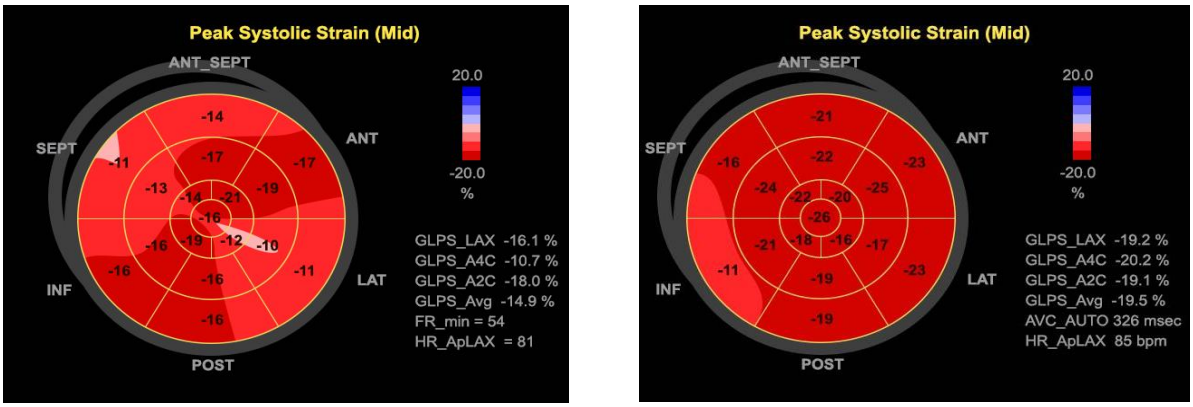

Figure (1) Bulls eye of global and segmental longitudinal strain in a dyslipidemic patient before the start of statin therapy (Left); GLS -16.1%, which improved after 6 months of statin – 19.2% (Right).

Discussion:

One of the major risk factors for the development of cardiovascular illnesses caused by atherosclerosis is dyslipidemia. It has a direct impact on the LV systolic function in addition to indirectly affecting heart function by encouraging the development of atherosclerosis and coronary artery disorders [2]. This direct effect could be explained by the slow accumulation of lipids in the heart, which can cause proinflammatory conditions, mitochondrial dysfunction, endothelial dysfunction that can lead to microvascular disorders, and fibrosis-related structural alterations in the heart [10].

Statins with frequent exercise can significantly lower the risk of cardiovascular death in individuals with dyslipidemia [4]. In addition to treating dyslipidemia, statin therapy offers additional advantages that happen at the cellular or molecular level [11]. Nevertheless, there is insufficient information regarding the presence of structural cardiac alterations in patients undergoing statin medication.

By comparing the global longitudinal systolic strain of dyslipidemic people with that of control subjects, our study aimed to identify subclinical left ventricular systolic dysfunction. We also wanted to evaluate how these characteristics were affected by a 6-month statin treatment.

There were 30 dyslipidemic participants in this study, 17 of whom were male (56.67 percent) and 13 of whom were female (43.33 percent). Thirty healthy individuals who were matched by age and sex were also present. The patients' ages ranged from 33 to 63 years, with 49 ± 9.19 years being the norm. This study's main results are that, as compared to control subjects, dyslipidemic people had a statistically significant impairment in their global longitudinal systolic strain prior to starting a statin (**Table ١**) and global longitudinal systolic

strain improvement that was statistically significant six months after starting statin medication (**Table ٣**).

To the best of our knowledge, this study is the first to assess global longitudinal systolic strain (GLSS) in dyslipidemic patients without additional risk factors both before and after short-term statin therapy.

In comparison between dyslipidemic patients prior to statin therapy and control participants, there was no statistically significant difference in ejection fraction (EF), with median values of 66.6 ± 5.9 and 68.0 ± 3.6, respectively (p value 0.4) (**Table ١**). Table 1 shows also that, nevertheless, there was a statistically significant difference in GLS between control and dyslipidemic patients prior to statin therapy (p value 0.015). Our results are similar to the fact that LVEF is not sensitive enough to detect minor changes in myocardial contractility, unlike myocardial strain generated by 2D speckle tracking.

This result was consistent with the research conducted by **Talini et al.**, which showed that individuals with hypercholesterolemia experience an early form of cardiac muscle dysfunction marked by inadequate heart contraction and relaxation [12]. Furthermore, **Rijswijk et al**. were able to show that a cohort of patients with cardiac steatosis had diastolic dysfunction when compared to a group of healthy individuals [13].

Moreover, our findings are consistent with other studies of a similar nature that have been carried out on patients with obesity and metabolic syndrome, though not particularly on the same population with dyslipidemia. Based on strain and strain-rate imaging, **Wang et al**. reported that patients with metabolic syndrome and normal left ventricular ejection fraction showed a slightly reduced regional left ventricular myocardial systolic performance [14].

Patients with dyslipidemia who had not started taking statins had significantly reduced global longitudinal systolic strain and segmental longitudinal systolic strain, as assessed by STE. The basal anterolateral, basal inferior, basal inferolateral, mid-inferolateral, and mid-anterior segments showed the greatest reduction. In comparison to the apical segments, the basal and mid-segments have a higher prevalence of affection. This mismatch could be explained by the longitudinal systolic strain in the mid- wall's natural propensity to be largest at the apex and lowest at the base [15]. Longitudinal systolic strain is considered an angle-independent method which has gained widespread recognition for its prognostic value [16].

This study discovered that the ejection fraction (EF) of dyslipidemic patients did not alter statistically significantly between the pre- and post-statin periods (**Table ٣**). Nonetheless, GLS (global longitudinal systolic strain) differed statistically significantly before and after statin medication combined with lifestyle changes (**Table ٣**). This result is consistent with the study carried out by **Jorgensen and colleagues** who concluded that there is a subtle reduction in left ventricular function as cholesterol remnants and triglyceride

levels increase. This suggests that these metabolites have an impact on cardiac systolic function that cannot be identified using traditional echocardiographic techniques but can be detected using global and segmental longitudinal systolic strain through speckle tracking echocardiography and longitudinal displacement through tissue Doppler [17].

This result is also consistent with the understanding that conventional metrics for myocardial function, such LVEF, are not sensitive to small changes in the heart and cannot detect early subclinical myocardial illness. **Bauersachs et al**. reported that statin therapy effectively restored impaired left ventricular function in rabbits following myocardial infarction. They further discussed the added protective effects observed in animals with normal cholesterol levels. Furthermore, it was suggested that the anti-inflammatory and anti-oxidative characteristics of simvastatin play a major role in its beneficial effects on heart function following myocardial infarction [18].

In Dahl salt-sensitive mice, atorvastatin treatment ameliorates cardiac fibrosis and improves left ventricular diastolic function, according to research by **Akahori et al**. [19]. This result is consistent with the study by **Talini et al**., which showed that people with hypercholesterolemia develop cardiomyopathy at an early age and that rosuvastatin may be able to correct systolic abnormalities [12].

Our results are consistent with those of **Moaref et al**., who found that asymptomatic individuals with metabolic syndrome and normal left ventricular ejection fraction (LVEF) have compromised global and segmental longitudinal systolic left ventricular strain, a measure of subclinical cardiovascular disease, as determined by speckle tracking echocardiography [20].

We speculate that global LV EF decline and overt heart failure, which may appear in patients with dyslipidemia, are preceded by the subclinical LV dysfunction linked to reduced GLS.

A comprehensive study conducted by **Nakagomi et al**., supported this theory. They discovered that statin drugs increase cardiac function and may help patients with dyslipidemia and congestive heart failure (CHF) have better long-term prognoses [21]. According to **Zhang et al**. meta-analysis; individuals with congestive heart failure (CHF) may see improvements in left ventricular remodeling, clinical symptoms, and cardiac performance when statin medicine is administered [22].

Our results, however, run counter to those of **Velagaleti et al** Framingham 's cohort study which looked into how lipid levels affect the anatomy of the heart and the incidence of heart failure. In the population they analyzed, they found a strong correlation between non-HDL and HDL cholesterol levels and the risk of heart failure [23]. As a result, it was determined that there was no meaningful relationship between LV structural alterations and serum lipid levels. However, no changes of diastolic and systolic function measures were analyzed by the researchers [24].

Additionally, the current study demonstrated that, following six months of statin therapy and lifestyle modifications, there was a statistically non-significant difference in EF between dyslipidemic patients and the control, with median values of 67.0 ± 4.6 and 68.0 ± 3.6, respectively, and p values of 0.48. **(Table ٤),** Moreover, six months after starting statin medication, there was a statistically non-significant difference (p = 0.55) between GLS in dyslipidemic patients and control **(Table ٤)**

Our hypothesis is that patients with dyslipidemia experienced subclinical cardiac systolic dysfunction, indicated by impaired GLSS, which resolved with the use of statin medication. This hypothesis is supported by the findings of **Wasim et al**., who found that statin medication has a variety of pleiotropic positive effects that are all cellular or molecular in nature. However, there is little data regarding structural cardiac alterations in statin therapy recipients [11]. The guanosine triphosphate (GTP-binding proteins), rat sarcoma virus (Ras), and Ras homolog family member A (Rho A) play a critical role in cardiac hypertrophy. Statins decrease their levels, cardiomyocyte hypertrophies, and fibrosis in wild type mice [10].

Statins have an impact on the myocardium by acting on Rho A and Rho-associated protein kinase (ROCK). This results in an increase in fibrosis and apoptosis, which may have a role in the development of left ventricular hypertrophy (LVH) and heart failure. Statin medication, however, lowers these components' levels. Furthermore, statins raise the level of nitric oxide (NO), which increases blood flow to the heart muscle in low oxygen environments and decreases the synthesis of vascular cell adhesion molecule-1 (VCAM-1), interleukins (IL)-6, and IL-8. In vitro laboratory investigations have demonstrated that statins can reduce mitochondrial dysfunction and cardiomyocyte mortality [25].

Even though the current study's results are encouraging, further extensive, multi-center clinical trials with long-term follow-up are required to validate our findings.

Conclusion:

Patients with dyslipidemia may have normal systolic function as determined by the EF technique, but they also have impaired global and segmental longitudinal systolic strain. This indicates the existence of subclinical left ventricular systolic dysfunction, which is improved by statins.

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