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ORIGINAL ARTICLE

The Significance of High-Sensitivity Cardiac Troponin T with Left Ventricular Strain in Heart Failure with Preserved Ejection Fraction

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ABSTRACT

Background: There is no enough information available at this time to determine if patients with stable heart failure and preserved ejection fraction also experience higher left ventricular strain and high-sensitivity troponin, which are associated with a worsening of the condition. **Aim:** To predict and early diagnose left ventricular dysfunction in patients with heart failure with preserved ejection fraction **Methods:** This case control study was conducted on 48 subjects diagnosed with heart failure with preserved ejection fraction (HFpEF), at Cardiology Department, Faculty of Medicine, Zagazig University. The patients were divided into 2 equal groups**:** case group (n=24): included patients diagnosed with HFpEF with diastolic dysfunction and control group (n=24): included healthy individuals. High-sensitivity cardiac troponin T and left ventricular strain were assessed in all subjects. **Results:** High sensitivity cardiac troponin T, GLS, GDS_{IVR}, GDS_{E}, SR_{E}, E/SR_{E} and SR_{IVR} were considerably greater in the cases group as opposed to the control group ($P<0.05$). **Conclusion:** In comparison to normal controls, our investigation revealed that HFpEF patients with diastolic dysfunction had significantly higher hs-cTnT levels, more severe abnormalities in left ventricular strain, and more advanced diastolic dysfunction.

Keywords: High-Sensitivity Cardiac Troponin T, Left Ventricular Strain, HFpEF.

INTRODUCTION

Heart failure (HF) represents a major public health concern in terms of morbidity and death concern that is growing more common and costly for the healthcare system **[1].** Over 26 million people worldwide suffer from heart failure (HF), which is linked to high rates of morbidity and mortality. The method most used to determine left ventricular ejection fraction (LVEF) is echocardiography. Remarkably, a sizable fraction of all HF patients or HFpEF, have clinical symptoms even while their LVEF is intact **[2].**

One of the main pathophysiological reasons for heart failure with a decreased ejection fraction (HFrEF) is cardiac injury. It has been shown that in both acute decompensation and stable outpatients with HF, routine and high-sensitivity troponin testing can identify continued myocardial damage **[3].**

Numerous hypothesized mechanisms, including increased protein turnover, Troponin release in heart failure (HF) has been associated with several factors such as myocardial ischemia from coronary artery disease or microcirculatory dysfunction, myocardial apoptosis or autophagy, damage caused by neurohormonal overactivation, and more. High-sensitivity (hs) testing may detect circulating troponin in about 100% of patients with stable chronic heart failure**.** Compared to the 99th percentile of hs-Tn for healthy people, this percentage is noticeably greater. 10% to 60% of patients may have circulating troponin identified using traditional techniques **[4].**

An essential part of diagnosing and treating acute coronary syndromes (ACS) is measuring circulating cardiac troponins (cTn). The importance of cTn measurement in ischemic heart disease and acute and chronic heart failure is being increasingly supported by studies **[5].**

The value of measuring patients' blood cardiac troponin with acute decompensated heart failure is

unclear. While a few restricted research indicate that elevated blood cardiac troponin levels are linked to unfavorable long-term consequences, the immediate consequences are not as well-defined **[6].**

In echocardiography, local myocardial shortening, thickness, and lengthening are referred to as regional left ventricular function (LV strain). The goal of strain is to use mechanical stress to gauge the level of wear and, consequently, the material's tension. It is needed to have a novel metric, such as LV strain, that can predict readmission and all-cause death within six months of discharge **[7,8].**

METHODS

This case control study was conducted on 48 subjects diagnosed with HFpEF, at Cardiology Department, Faculty of Medicine, Zagazig University. Written informed consent was obtained from all participants, the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University (IRB ١٠٨٣٣). The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Two equal groups were formed out of the patients: Twenty-four patients with HFpEF and diastolic dysfunction made up the case group, and twenty-four healthy people made up the control group.

Inclusion criteria comprised patients having a diagnosis of HFpEF and those who were at least 18 years old. Following a baseline diagnostic work-up, the patients' condition was diagnosed with HFpEF in compliance with the guidelines of heart failure of the European Society of Cardiology (ESC)**[9].**

Exclusion criteria: Patients had poor echocardiographic imaging and more than mild calcification or regurgitation of the mitral valve, high-grade atrioventricular block, acute coronary syndrome, significant comorbidities, atrial fibrillation, or ventricular pacing. Images with missing apical views, poor quality images, low frame rates (<50 frames per second), inadequate myocardial wall visibility or traceability during the cardiac cycle in more than two segments in a single view or patients not accepted for the study were excluded from analysis according to standard operating procedure.

Every patient underwent the following procedures: a complete history, a full clinical examination, the NYHA Functional Class, a complete blood count, testing for the kidneys, liver, and kidneys, and a Hs-Troponin T test.

Echocardiography:

Standard 2D transthoracic echocardiogram (2D TTE) was performed on all patients utilizing a single ultrasound equipment that was equipped with specialized speckle-tracking analytic software. The standard for measuring traditional echocardiographic parameters was set by the American Society of Echocardiography (ASE) [10]. A calculation of the left ventricular ejection fraction (LVEF) was made using the apical four-chamber and two-chamber viewpoints using the Biplane disk assumption technique. EF (%) = [(End-diastolic volume (EDV) - end-systolic volume (ESV) / EDV] x 100 [10]. The diastolic transmitral flow velocities (E, A) utilising a pulsed-wave doppler, were measured in the apical four-chamber view. Tissue Doppler Imaging (TDI) was used to assess the diastolic mitral annular velocities (e', a') in the same picture. The sample volume was positioned at the lateral and septal annuli in order to calculate the average e' **[10].** A 1.5 mm sample volume was positioned at the mitral annulus' leaflet origin during TDI **[11].** Background noise is eliminated with proper gain and filter changes. To prevent angle dependency in tissue Doppler measurements, we maintained an angle of greater than 15 between the PW-Doppler beam and the wall's movement direction. The lateral and septal locations were used to quantify the systolic (S′), early (E′), and late (A′) diastolic peak velocities. As a result, for every patient, the early to late annular velocity (E′/A′) and the transmitral flow velocity to annular velocity ratio (E/E′) were calculated. Conventional methods, such the left atrial volume index (LAVI), were employed to assess the chamber measurements **[12].**

Assessment of Diastolic Dysfunction Grade

Diastolic dysfunction grade was determined using echocardiographic parameters according to ASE guidelines **[13]:**

Mitral Inflow Velocities:

- E wave = peak early diastolic mitral inflow velocity
- A wave = peak late diastolic mitral inflow velocity during atrial contraction

Mitral Annular Tissue Doppler Velocities:

- e' = early diastolic mitral annular velocity representing myocardial relaxation

Additional Parameters:

- Left atrial volume index (LAVi)
- Peak tricuspid regurgitation velocity

Strain Imaging:

LV strain parameter (global longitudinal strain, or GLS) was computed by the widely used method of speckle tracking echocardiography. Grey-scale acquisition was used to record three cardiac cycles at a frame rate higher than 80s from the long-axis, two-chamber, and apical perspectives. The standard ECHOPAC tool for two-dimensional (2D) strain analysis was used to construct a strain rate curve and global longitudinal strain that encompassed all LV myocardial segments in each image **[14].** From three apical viewpoints (three-chamber, four-chamber, and two-chamber), the average peak values of 17

segmental longitudinal stresses were used to calculate GLS. The LV endocardial border was physically traced before the LV strain parameters were automatically computed using specialized software. The frame rate was from 60 to 100 fps. Similarly, SRE and during SRIVR were determined. E/SRIVR was also calculated.

STATISTICAL ANALYSIS

We used SPSS v28 for statistical analysis. Quantitative variables, unpaired Student's t-test was used to compare the mean and standard deviation (SD) of the two groups. The Fisher's exact test or, if applicable, the Chi-square test was used to look at the frequency and percentage (%) of the qualitative variables. Measures included the Receiver Operating Characteristic curve (ROC-curve), spearman correlation, and Pearson correlation.

RESULTS

The case and control groups' ages differed in a statistically meaningful way (P<0.001). There were negligible differences in the other baseline parameters (sex, weight, height, Body Mass Index (BMI), body surface area, and smoking) between the two groups. In terms of risk variables, the case group's history of Myocardial infarction (MI), Chronic obstructive pulmonary disease (COPD), renal failure, diabetes mellitus, and hypertension were significantly greater than those of the control group. **[Table 1Error! Reference source not found.]**

As demonstrated in **Table 2,** NYHA class was significantly different between both groups. New York Heart Association (NYHA) class was class 1 in 25% of cases, class 2 in 16.67%, class 3 in 41.67% and class 4 in 16.67% of cases while it was class 1 in all controls.

There was no significant difference in heart rate, there were significant difference in systolic blood pressure (SBP) and Diastolic blood pressure (DBP) between the studied groups, with cases having greater SBP and DBP than controls. **[Table 3]**

In comparison to the control group, the case group's serum creatinine and hs-cTn were significantly greater (P=0.015, <0.001). Other laboratory findings (Hemoglobin (Hb), white blood cells, Platelet count, urea, alanine transaminase and aspartate aminotransferase) were insignificantly different between both groups. **[Table 4Error! Reference source not found.]**

Significant variations (P<0.05) were observed in the echocardiography results between the case and control groups in terms of tricuspid regurgitation peak velocity, left atrial volume (LAV), LAVI, E wave, A wave, E/A ratio, deceleration time, Lateral e' E/lateral e' ratio, E/e' average, and E/septal e' ratio. Septal e' significantly decreased in the case group compared to the control group (P=0.002, <0.001). But as far as EF was concerned, nothing changed. Diastolic dysfunction in the case group was categorized into three grades: grade I affected seven patients (29.17%), grade II affected fourteen patients (58.33%), and grade III affected three patients (12.5%). **[Table 5]**

According to the results of the speckle tracking echocardiogram, the case group outperformed the control group in terms of GLS, GDSIVR, GDSE, SRE, E/SRE, and SRIVR (P<0.05). E/SRIVR did not significantly differ between the two groups. **[Table 6]**

Age, SBP, DBP, LAV, LAVI, E wave, A wave, E/A ratio, deceleration time, lateral e', E/lateral e' ratio, E/e' average, E/septal e' ratio, tricuspid regurgitation peak velocity, GLS, GDSIVR, GDSE, SRE, and E/SRE were among the characteristics with which hs-cTn showed significant positive associations. The following metrics showed substantial negative relationships with hs-cTn: septal e. The associations between high-sensitivity cardiac troponin (hs-cTn) and the other parameters were not statistically significant. **[Table7]**

Table 1: Baseline characteristics of the studied groups

		Case group (n=24)	Control group (n=24)	P value
Age (years)	**Mean± SD**	72.04 ± 4.11	60.8 ± 5.28	**<0.001***
	Range	65 - 80	50 - 70	
Sex	**Male**	3 (12.5%)	9 (37.5%)	0.093
	Female	21 (87.5%)	15 (62.5%)	
Weight (Kg)	**Mean± SD**	70.6 ± 8.45	71.0 ± 8.84	0.868
	Range	55 - 83	55 - 85	
Height (m)	**Mean± SD**	1.6 ± 0.06	1.6 ± 0.06	0.942

		Case group (n=24)	Control group (n=24)	
	Range	1.55 - 1.75	1.55 - 1.75	
BMI (Kg/m^2)	**Mean± SD**	26.4 ± 3.78	26.6 ± 4.26	0.895
	Range	19.49 - 33.67	19.92 - 35.38	
BSA (ml/m^2)	**Mean± SD**	1.8 ± 0.12	1.8 ± 0.11	0.677
	Range	1.59 - 2	1.55 - 1.96	
Smoking		10 (41.67%)	6 (25%)	0.220
Hypertension		13 (54.17%)	0 (0%)	**<0.001***
Diabetes mellitus		8 (33.33%)	0 (0%)	**<0.001***
Renal failure		8 (33.33%)	0 (0%)	**<0.001***
COPD		12 (50%)	0 (0%)	**<0.001***
History of MI		7 (29.17%)	0 (0%)	**<0.001***

BMI: body mass index, BSA: body surface area, COPD: chronic obstructive pulmonary disease, MI: myocardial infarction, *: statistically significant as p value <0.05.

Table 2: Clinical symptoms of the studied groups

		Case group (n=24)	Control group (n=24)	P value
NYHA class	**1**	6 (25%)	24 (100%)	**<0.001***
	2	4 (16.67%)	0 (0%)	
	3	10 (41.67%)	0 (0%)	
	4	4 (16.67%)	0 (0%)	

NYHA: New York Heart Association

Table 3: Clinical examination of vital signs of the studied groups

		Case group (n=24)	Control group (n=24)	P value
SBP (mmHg)	**Mean± SD**	127.9 ± 12.85	120.5 ± 4.1	**0.01**
	Range	110 - 150	110 - 125	
DBP (mmHg)	**Mean± SD**	81.7 ± 7.02	75.5 ± 4.24	**0.001**
	Range	70 - 90	70 - 80	
HR (beats/min)	**Mean± SD**	83.5 ± 7.07	80.3 ± 5.1	0.07
	Range	71 - 95	71 - 87	

SBP: systolic blood pressure, DBP: diastolic blood pressure, HR: heart rate.

Table 4: Laboratory investigations of the studied groups

		Case group (n=24)	Control group (n=24)	P value
Hb (g/dL)	**Mean± SD**	11.4 ± 0.98	11.3 ± 0.88	0.793
	Range	10 - 13	10.2 - 12.9	
PLT (*10^9/L)	**Mean± SD**	234.3 ± 37.17	242.6 ± 36.13	0.43
	Range	171 - 289	176 - 290	
WBCs (*10^9/L)	**Mean± SD**	7.2 ± 1.74	7.7 ± 1.57	0.293
	Range	4.7 - 10.2	4.5 - 10.4	
Serum creatinine (mg/dL)	**Mean± SD**	1.7 ± 1.32	0.9 ± 0.88	**0.015***
	Range	0.5 - 4.3	0.5 - 4.5	
Urea (mg/ dL)	**Mean± SD**	49.6 ± 13.71	49.96 ± 11.7	0.928
	Range	30 - 68	25 - 69	
ALT (U/L)	**Mean± SD**	26.1 ± 7.08	26.5 ± 6.89	0.853
	Range	15 - 36	15 - 38	

		Case group (n=24)	Control group (n=24)	P value
AST (U/L)	**Mean± SD**	30.1 ± 5.67	28.5 ± 6.3	0.353
	Range	21 - 40	20 - 40	
hs-cTn (ng/mL)	**Mean± SD**	17.7 ± 6.62	0.009 ± 0.003	**<0.001***
	Range	7.7 - 27.1	0.002 – 0.013	

Hb: hemoglobin, PLT: platelets, WBCs: white blood cells, ALT: alanine aminotransferase, AST: aspartate aminotransferase, hs-cTn: high-sensitivity cardiac troponin, *: statistically significant as P value <0.05.

Table 5: Echocardiography of the studied groups

		Case group (n=24)	Control group (n=24)	P value
EF (%)	**Mean± SD**	60.4 ± 5.19	61.96 ± 4.73	0.28
	Range	56 - 66	56 - 67	
LAV (ml)	**Mean± SD**	64.6 ± 11.44	29.8 ± 3.07	**<0.001***
	Range	44 - 83	22.4 – 33.5	
LAVI (mL/m^2)	**Mean± SD**	44.2 ± 4.82	24.2 ± 2.5	**<0.001***
	Range	37 - 53	21 - 27	
E wave (cm/s)	**Mean± SD**	87.1 ± 11.63	67.1 ± 6.32	**<0.001***
	Range	68 - 107	60 - 79	
A wave (cm/s)	**Mean± SD**	87.6 ± 14.1	44.2 ± 6.7	**<0.001***
	Range	62 - 111	23 - 54	
E/A ratio	**Mean± SD**	1.02 ± 0.21	0.92 ± 0.1	**0.041***
	Range	0.68 - 1.5	0.8 - 1.1	
Deceleration time (ms)	**Mean± SD**	212 ± 16.41	186.4 ± 24.38	**<0.001***
	Range	190 - 240	160 - 215	
Lateral e` (cm/s)	**Mean± SD**	10.8 ± 1.2	8.6 ± 0.83	**<0.001***
	Range	8 - 12	6.5 - 9.9	
Septal e` (cm/s)	**Mean± SD**	5.3 ± 0.44	7.7 ± 0.61	**<0.001***
	Range	4.8 - 6.2	7 - 8	
E/lateral e` ratio	**Mean± SD**	11.3 ± 1.97	7.9 ± 1.18	**<0.001***
	Range	8.47 - 14.56	6.18 - 10.27	
E/e` average	**Mean± SD**	13.1 ± 1.65	7.5 ± 0.86	**<0.001***
	Range	10.8 - 16.1	7.1 - 7.9	
E/septal e` ratio	**Mean± SD**	16.4 ± 2.1	8.8 ± 0.93	**<0.001***
	Range	12.41 - 20.42	7.05 - 10.58	
Tricuspid regurgitation peak velocity (m/s)	**Mean± SD**	2.9 ± 0.32	2.3 ± 0.2	**<0.001***
	Range	2.5 - 3.5	2.2 - 2.4	
Grade of diastolic dysfunction	**Grade I**	7 (29.17%)	0 (0%)	---
	Grade II	14 (58.33%)	0 (0%)	
	Grade III	3 (12.5%)	0 (0%)	

EF: ejection fraction, LAV: left atrial volume, LAVI: left atrial volume index, E: peak early diastolic mitral inflow velocity, e′: mitral annulus early diastolic velocity, *: statistically significant as P value <0.05.

Table 6: Speckle tracking echocardiography of the studied groups

		Case group (n=24)	Control group (n=24)	P value
GLS (%)	**Mean± SD**	-18 ± 2.18	-22 ± 0.91	**<0.001***
	Range	-21 – (-15)	-23 – (-21)	
GDS_{IVR}	**Mean± SD**	-15.9 ± 0.9	-19.5 ± 0.46	**<0.001***
	Range	-17 – (-15)	-20 – (-19)	
GDS_E	**Mean± SD**	-17.2 ± 0.7	-19.6 ± 1.5	**<0.001***

		Case group (n=24)	Control group (n=24)	
	Range	-18 – (-16)	-21 – (-18)	
SR_E	**Mean± SD**	0.37 ± 0.14	0.08 ± 0.01	**<0.001***
	Range	0.13 – 0.60	0.07 – 0.087	
SR_{IVR}	**Mean± SD**	-0.1 ± 0.14	-0.24 ± 0.07	**<0.001***
	Range	-0.29 - 0.14	-0.23 – (-0.25)	
E/SR_E	**Mean± SD**	482.1 ± 60.25	392.5 ± 70.51	**<0.001***
	Range	396 - 584	305 – 480	
E/SR_{IVR}	**Mean± SD**	-376.3± 282.7	-530 ± 53.1	0.21
	Range	-816 - 21	-640 – (-421)	

GLS: global longitudinal strain, GDS_{IVR}: global diastolic strain in in isovolumetric relaxation, GDS_E: global diastolic strain in early filling, SR_E: strain rate during early filling, SR_{IVR}: strain rate during isovolumic relaxation, E/SR_E: mitral pulsed doppler early filling/ strain rate in early filling, E/SR_{IVR}: mitral pulsed doppler early filling/ strain rate in in isovolumetric relaxation. *: statistically significant as P value <0.05.

Table 7: Correlation between hs-cTn and different parameters

	hs-cTn (ng/mL)	
	r	**p**
Age (years)	0.647	**<0.001***
Sex	0.181	0.219
Weight (Kg)	-0.115	0.436
Height (m)	-0.099	0.505
BMI (Kg/m^2)	-0.048	0.744
BSA (ml/m^2)	-0.192	0.224
History of MI	-0.086	0.561
NYHA class	0.039	0.794
SBP (mmHg)	0.548	**<0.001***
DBP (mmHg)	0.484	**<0.001***
HR (beats/min)	0.151	0.307
Hb (g/dL)	0.225	0.125
PLT ($*10^9/L$)	-0.282	0.052
WBCs ($*10^9/L$)	-0.189	0.198
S. creatinine (mg/dL)	0.201	0.171
Urea (mg/dL)	-0.027	0.857
ALT (U/L)	0.028	0.849
AST (U/L)	0.169	0.252
EF (%)	0.101	0.342
LAV (ml)	0.563	**0.005***
LAVI (mL/m^2)	0.715	**<0.001***
E wave (cm/s)	0.678	**<0.001***
A wave (cm/s)	0.434	**0.002***
E/A ratio	0.345	**0.016***
Deceleration time (ms)	0.436	**0.002***
Lateral e` (cm/s)	0.574	**0.001***
Septal e` (cm/s)	-0.764	**<0.001***
E/lateral e` ratio	0.695	**<0.001***
E/e` average	0.804	**<0.001***
E/septal e` ratio	0.806	**<0.001***
Tricuspid regurgitation peak velocity (m/s)	0.667	**<0.001***
GLS (%)	0.657	**<0.001***
GDS_{IVR}	0.734	**<0.001***

	hs-cTn (ng/mL)	
	r	r
GDS_E	0.552	**<0.001***
SR_E	0.471	**<0.001***
SR_{IVR}	0.178	0.227
E/SR_E	0.420	**0.003***
E/SR_{IVR}	-0.19	0.197

r: correlation coefficient, BMI: body mass index, BSA: body surface area, NYHA: New York Heart Association, SBP: systolic blood pressure, DBP: diastolic blood pressure, HR: heart rate, Hb: hemoglobin, PLT: platelets, WBCs: white blood cells, ALT: alanine aminotransferase, AST: aspartate aminotransferase, hs-cTn: high-sensitivity cardiac troponin, GLS: global longitudinal strain, GDSIVR: global diastolic strain in in isovolumetric relaxation, GDSE: global diastolic strain in early filling, SRE: strain rate during early filling, SRIVR: strain rate during isovolumic relaxation, E/SRE: mitral pulsed doppler early filling/ strain rate in early filling, E/SRIVR: mitral pulsed doppler early filling/ strain rate in isovolumetric relaxation. *: statistically significant as p value <0.05.

DISCUSSION

The two groups in our study had similar body mass indexes (Mean± SD=26 Kg/m2), sex distributions, weights, and heights. On the other hand, the case group's mean age was 72.04 ± 4.11 years against 60.8 ± 5.28 years (p<0.001), much older than the control group. In both categories, there was a preponderance of females (87.5%; 62.5%).

In terms of risk factors, the case group in our study had significantly greater rates of hypertension, diabetes mellitus, renal failure, COPD, and a history of MI than the control group.

As a result, **Kerstens et al. [9]** aimed to examine the connection between strain-volume loops (SVL) characteristics and adverse outcomes in HFpEF.. They said that the BMI of HFpEF patients (72.3% female) was 29.9 ± 5.4 kg/m2, and their age was 75.8 ± 6.9.

In agreement, **Kerstens et al. [9]** noted that HFpEF patients compared to controls, were somewhat older, more frequently female, and more likely to have a medical history of atrial fibrillation and hypertension.

In our study, hs-cTnT levels were significantly greater in diastolic dysfunction patients with HFpEF (mean 17.7 ng/mL) than in normal control patients (mean 0.009 ng/mL) (p<0.001).

This is in line with the research conducted by **Suzuki et al. [15],** which examined elevated-sensitivity troponin T (hs-TnT) as a predictive measure for heart failure patients with preserved ejection fraction (HFpEF). Comparing the results to the control group, it was discovered that those who were experiencing unpleasant events had significantly greater levels of Hs-TnT (p = 0.003).

This outcome is in line with the findings of **Jhund et al. [16],** who discovered that most patients had hs-TnT concentrations above the cutoff point required to detect cardiac damage. Increased hs-TnT levels were associated with certain features, such as cardiac structural abnormalities, that have been associated with worse outcomes in individuals with HFpEF.

Myhre et al. found a strong correlation between participants' levels of high-sensitivity cardiac troponin T (hs-cTnT) and their degree of diastolic dysfunction **[17].** Notably, it was shown that people with higher hs-cTnT levels and diastolic dysfunction were statistically substantially more prone to have one of the two conditions than not to have either.

49% of patients in the Controlled Rosuvastatin Multinational Trial in HF (CORONA) had hs-TnT levels over the threshold (0.014 µg/L) for the detection of myocardial damage using a Roche test **[18].**

Utilising a Roche hs-TnT assay, 47% and 64% of the participants in the Valsartan Heart Failure Trial (Val-HeFT) and Gruppo Italiano per lo Studio della Sopravvivenza nell'Insufficienza Cardiaca-Heart Failure trial (GISSI-HF) had hs-TnT levels above the limit of detection for myocardial injury (0.0135 µg/L), respectively **[19].**

Conversely, in a population-based study included men and women aged 54 to 74, 7.4% of individuals had hs-TnT in the range of cardiac injury (>0.014 µg/L) **[20].**

The primary cause of troponin increase in acute coronary syndrome is myocyte cell death. The pathophysiological processes of subendocardial ischemia, neurohormonal activation, inflammatory cytokine release, altered calcium management, oxidative stress, and increased wall stress are responsible for myocardial damage and the rise in

troponin in HFpEF. Cardiac troponin exhibits a strong correlation with unfavorable cardiac events under these pathways **[21].**

Ventricular diastolic dysfunction (diastolic stiffness and poor relaxation) is commonly observed in HFpEF and can be triggered by stressors such as exercise, tachycardia, or hypertension, or it can occur spontaneously **[22].** Common conditions include increased ventricular systolic stiffness, vascular stiffening, and endothelial dysfunction **[23].** One other mechanism that has been postulated recently to lead to changes in cardiomyocyte signaling pathways and cardiac inflammation and fibrosis is systemic microvascular endothelial inflammation associated with comorbid diseases. Among these alterations include elevations in oxidative stress **[25],** rarefaction and microvascular dysfunction in cardiac and skeletal muscle **[24],** and abnormalities in cell remodeling. Given these circumstances, an increase in troponin in HFpEF may be a sign of microvascular endothelial inflammation that causes myocardial mortality and the fibrosis that follows. But more research is required because this theory is still theoretical **[23].**

The case group's echocardiogram results ($P<0.05$) compared favorably to the control group in terms of LAV, LAVI, E wave, A wave, E/A ratio, deceleration time, Lateral e', E/lateral e' ratio, E/e' average, E/septal e' ratio, and peak velocity of tricuspid regurgitation. Septal e' significantly decreased in the case group compared to the control group ($P=0.002$, <0.001). But as far as EF was concerned, nothing really changed.

Early diastolic characteristics, including E/e′, have also been linked in earlier research to unfavorable outcomes in HFpEF **[26]**.

Measuring myocardial stiffness (such as LV late diastolic pressures or deceleration time) and myocardial relaxation (such as Examining diastolic function from a mechanistic approach usually requires left ventricle (LV) systolic pressure fall or mitral annulus early diastolic velocity (e′) **[27].** It is well recognised that HFpEF affects LV stiffness, which is frequently assessed late in diastole **[28].** Furthermore, it has been demonstrated that echocardiographic indicators of early diastole are highly reliable in predicting the diagnosis of HFpEF [**29].**

According to our analysis, 7 patients (29.17%), 14 patients (58.33%), and 3 patients (12.5%) in the case group exhibited grade I, grade II, and grade III diastolic dysfunction.

Our results are in line with those of **Wenzel et al. [30],** who examined the frequency of DD and its associations in people with and without HFpEF in a middle-aged general population sample. Their results showed that 1.3% of DD patients developed overt HFpEF, while the remaining DD subjects (11.5%) showed no symptoms.

Our study significantly abnormal global longitudinal strain (GLS), early diastolic strain rate (SRIVR), and strain (GDSIVR and GDSE) values in HFpEF patients with diastolic dysfunction.

The abnormal strain patterns agree with previous echocardiographic evaluations in HFpEF **[31].** It suggests diastolic dysfunction in HFpEF is associated with reduced myocardial relaxation and compliance. Troponin levels correlated significantly with strain abnormalities as well, again pointing to related myocardial injury.

Kerstens et al. [9] demonstrated a substantial difference in the strain-volume loop (SVL) features between the two groups, in comparison to the control group, patients with DD showed significantly more early and late diastolic "uncoupling." This indicates that the link between longitudinal strain and diastolic and volume differs from the systolic relationship. Put another way, for a given change in volume, the LV exhibits less longitudinal deformation early in diastole. There were no variations in systolic features (such as peak strain) across the groups, however these variations in loop characteristics were notably seen during diastole.

Hulshof et al. [32] reported that patients with aortic regurgitation and aortic stenosis had higher levels of uncoupling. Following aortic valve replacement, variations in uncoupling were also significantly linked with cardiac remodeling. **Pagourelias et al. [33]** reported a larger uncoupling in hearts that may be stiffer in hypertrophic cardiomyopathy. Interestingly, **Hubert et al. [34]** found that patients with HFpEF and amyloidosis had a smaller region encompassed by the SVL than healthy controls.

Impairment of LV GLS was reported to be frequent, affecting 65% of the sample population, by **DeVore et al. [35].** Poor left ventricular filling, which is closely associated with objective measurements of deficient increased wall stress, ventricular filling, and myocardial fibrosis, but not with functional capacity or quality of life, is a common feature of most patients with HFpEF.

Luvsansuren and Chimed [36] reported that patients with and without clinical heart failure had significantly different left ventricular global strains

($p<0.001$) (−11.1±1.85% vs. −16.6±3.38%) In **Tah et al. [37]** study, speckle tracking strain analysis provided complementary value to conventional diastolic parameters like annular e' velocities for discriminating diastolic dysfunction severity. Strain imaging has prospect for better phenotyping HFpEF patients, as supported by past studies.

The following parameters showed significant positive correlations with hs-cTn in our study: tricuspid regurgitation peak velocity, GLS, GDSIVR, GDSE, SRE, E/SRE, E wave, A wave, E/A ratio, deceleration time, lateral e', E/lateral e' ratio, E/e' average, and E/septal e' ratio. The following factors showed strong negative relationships with hs-cTn: septal e'. The associations between hs-cTn and the other parameters were not statistically significant. This is consistent with the findings of **Suzuki et al. [15],** who found that Hs-TnT substantially linked with age but not with sex or hemoglobin.

Elevated troponin levels are thought to reflect greater myocardial injury and stress in these patients **[38].** The significant positive correlations found here between hs-cTnT and parameters like LA volume index and E/e' ratio support this. In patients suffering from severe diastolic dysfunction, **Hoffmann et al. [39]** found a substantial association between TnT values and echocardiographic indications of LV hypertrophy.

Myhre et al. [17] report strong correlation between hs-cTnT levels and diastolic function indicators in these elderly people, such as TDI e′, E/e′ ratio, and LA size, particularly when hs-cTnT concentrations are within the normal range. In their investigation, the global longitudinal strain and LVEF of an older adult population free of cardiovascular disease and with significantly sustained LVEF were correlated with higher concentrations of hs-cTnT in unadjusted analysis.

Systolic metrics (LVEF and mitral annular plane systolic excursion) and cardiac troponin have been correlated in patients with heart failure in the past **[40].**

In an adjusted model, increased hs-TnT was linked to diastolic dysfunction and left ventricular hypertrophy (LVH) at baseline, but not systolic dysfunction, according to **Kang et al. [41].**

CONCLUSION

Our study found HFpEF patients with diastolic dysfunction had significantly higher hs-cTnT levels, more severe abnormalities in left ventricular strain, and more advanced diastolic dysfunction compared to normal controls. Hs-cTnT and strain parameters were closely associated with diastolic dysfunction severity. For the early diagnosis, prognosis, and detection of myocardial dysfunction in HFpEF, these biomarkers may be helpful.

CONFLICTS OF INEREST

The authors report no conflicts of interest. The authors along are responsible for the content and writing of the paper.

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