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ORIGINAL ARTICLE

The Value of Post-Exercise Electrocardiography and Troponin I Serum Level in Women with Angina with Non Obstructive Coronary Artery Disease

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ABSTRACT

Background: Angina with non-obstructive coronary artery disease (ANOCA) is increasingly recognized as a cause of chest pain. Post-exercise electrocardiography (ECG) and serum cardiac biomarkers such as troponin I may provide additional value in detecting myocardial ischemia and stratifying risk in this population. So, Our goal was to determine whether myocardial damage was present in women with non-obstructive CAD based on elevated troponin-I levels and how it related to coronary flow and left ventricular longitudinal strain.

Methods: This prospective cohort study was conducted at department of Cardiology, Faculty of Medicine, Zagazig University on women presented for coronary angiography due typical angina chest pain and documented to have normal coronary or non-significant coronary stenosis. Post-exercise electrocardiography and troponin-I were measured in all patients.

Results: In this study, women with subclinical systolic dysfunction (mean age 52.00±6.81 years) had higher diabetes prevalence (55.6% vs. 25.0%, p=0.036), greater basal DBP (p=0.023), higher peak HR (p=0.008), larger LAVI (33.64±6.42 vs. 28.30±7.37 mL/m², p=0.011), increased E/e′ ratio (13.36±3.99 vs. 9.77±4.70, p=0.007), and reduced GLS (14.22±1.48% vs. 21.10±2.22%, p < 0.001). Post-exercise hs-TnT was elevated (20.68±9.20 vs. 12.23±8.30 ng/L, p=0.002). Troponin increase predicted dysfunction (AUC=0.743, 95% CI: 0.594–0.859; cutoff >12.6 ng/L; sensitivity 70.37%, specificity 75.00%; p=0.0015).

Conclusion: Subclinical systolic dysfunction in women with non-obstructive CAD is strongly linked to post-exercise troponin elevation, predicting dysfunction with good diagnostic accuracy. Integrating troponin testing with strain imaging enhances early detection, risk stratification, and timely management in women with angina and preserved ejection fraction.

Keywords: Angina; Non-obstructive coronary artery disease; Post-exercise ECG; Troponin I.

INTRODUCTION

In individuals with and without documented coronary artery disease, elevated cardiac troponin (cTn), a sign of myocardial injury, is linked to a poor prognosis **[1].** Despite the fact that cardiovascular disease affects both men and women, there aren't many age- and sex-specific imaging and therapy guidelines for women with cardiovascular disease **[2].**

Despite presenting at an older age and carrying a larger burden of risk factors than males, women are more likely to have angina but less likely to have atherosclerosis and obstructive CAD **[3].**

The traditional diagnostic objective of identifying obstructive CAD that requires revascularization is challenged by the higher prevalence of non-obstructive CAD in women, which causes the focus to change to identifying ischemia **[4].**

According to the Women's Ischemia Syndrome Evaluation (WISE) research, many women who

come with chest pain have signs of exercise-induced myocardial ischemia and coronary vasomotor dysfunction, which presents diagnostic problems even in the absence of obstructive coronary atherosclerosis **[5].**

When referred for an invasive coronary assessment, women who exhibit symptoms and signs of ischemia frequently show no indicators of obstructive coronary artery disease (CAD) **[6].** According to studies, people with non-obstructive CAD who exhibit symptoms are more likely to experience negative outcomes and die from all causes than those who do not exhibit any symptoms or indications of ischemic heart disease **[7].**

Clearly, increased cTnT is a sign of myocardial damage. However, a number of studies have shown that cTnT increases following brief ischemia episodes as well. The prevalence of high cTnT in NOCAD patients and its importance in women with angina and no obstructive coronary artery disease are, however, little understood **[8].**

We hypothesized that post exercise elevation of troponin-I is associated with subclinical systolic dysfunction and impaired myocardial coronary flow in women with non-obstructive CAD and preserved ejection fraction, thus we aim to assess the occurrence of myocardial injury by elevated troponin- I levels and its relation with left ventricular longitudinal strain and coronary flow in women with non-obstructive CAD.

METHODS

This prospective cohort study was conducted at Department of Cardiology, Faculty of Medicine, Zagazig University on 48 women who were presented for coronary angiography due to typical angina chest discomfort and documented to have normal coronary or non-significant coronary stenosis. All recruited patients had a good left ventricular ejection function (LVEF > 50%), **Figure 1S**. The Zagazig University Faculty of Medicine's ethical committee gave its approval to the investigation. (IRB 377-4-June-2024). An informed written consent was obtained from all patients.

Exclusion criteria included significant coronary artery stenosis, acute coronary syndromes, valvular heart disease, LVEF less than 50%, sever liver impairment, patients with interstitial lung disorders, COPD, severe renal impairment (eGFR < 30 ml/min), and any other serious co-morbid conditions that significantly shorten the patient's life expectancy.

Sample size justification: Assuming that rate of admission of CAD patients at ZHU is 8 cases/month. So, a consecutive sample of 48 cases were included in our study.

Every patient underwent a thorough history taking, a general examination, and standard laboratory testing.

12-lead ECG

It was done to show any Rhythm disturbances and evaluation of resting ECG changes:

• A brief history of medication use and adhesive gel allergies was taken. Electrodes with adhesive gel were applied after removing all metallic items. The patient was positioned supine before recording.

Exercise Treadmill Testing

All patients underwent symptom-limited treadmill testing using the standard Bruce protocol. A 12-lead ECG was recorded before exercise, at the end of each stage, at peak effort, and every 2 minutes during recovery, while three leads were continuously monitored. The test was stopped for limiting symptoms (angina, dyspnea, exhaustion), abnormal blood pressure or rhythm, or progressive ST deviation (>0.2 mV with typical angina or during the first exercise stage). A positive test was defined as exercise-induced ST depression ≥1 mm at 0.06 s after the J point relative to the PR segment. The supervising clinician distinguished exercise-induced angina from nonanginal pain based on reproduced symptoms and classical angina features.

Duke Treadmill Score:

The Duke Treadmill Score (DTS) is calculated as: exercise duration in minutes − (5 × ST deviation) − (4 × exercise angina), where angina is graded as 0 for none, 1 for nonlimiting, and 2 for exercise-limiting. ST deviation is defined as the maximum elevation

or depression observed in any lead except aVR. The score typically ranges from −25 to +15 and is used to stratify risk: scores ≥ +5 indicate low risk, scores between −10 and +4 indicate moderate risk, and scores < −11 indicate high risk **[9].**

Assessment of cardiac Troponin I Serum Level

To determine serum TnT levels, blood samples were collected from the antecubital vein at admission. The first sample (cTnT-1) was obtained immediately after the treadmill test, and the second (cTnT-2) 12 hours later. Samples were stored at 4°C for up to 24 hours and analyzed using the hs-cTnT STAT assay on the Architect SR2000i (Abbott Diagnostics, Abbott Park, IL, USA). The assay's detection limit was 1.6 ng/L, with a 99th percentile cutoff of 29 ng/L. The longitudinal change in cTnT over 24 hours was calculated as cTnT-1 concentration minus cTnT-2 concentration **[10].**

Coronary angiography with TIMI flow assessment

Coronary angiography was performed using a 4F catheter via the right femoral route, with images obtained in 30° right anterior oblique and 60° left anterior oblique views. Stenosis severity was expressed as the percentage reduction in luminal diameter relative to an adjacent reference segment: non-obstructive CAD (<50%), mild stenosis (<30%), and moderate stenosis (30–49%). Coronary blood flow was evaluated using the standard Thrombolysis in Myocardial Infarction (TIMI) grading system: TIMI 0 (no perfusion) indicates no antegrade flow beyond the occlusion; TIMI 1 (penetration without perfusion) reflects minimal distal filling without complete opacification; TIMI 2 (partial perfusion) denotes delayed but complete opacification of the distal bed with slow clearance; and TIMI 3 (complete perfusion) represents normal, rapid opacification and clearance comparable to non-diseased vessels.

Echocardiographic Evaluation

Left ventricular stroke volume (LVSV) was assessed in each participant using six techniques: forward stroke volume by Doppler echocardiography, M-Mode analysis with the Teichholz formula (LVSVM-Mode: $V = 7\times D^3/(2.4 + D)$), manual Simpson biplane 2D planimetry (LVSV biplane), simultaneous triplane planimetry (LVSV triplane), and 3D volumetry with manual correction (LVSV 3D-volumetry). In addition, the LVOT cross-sectional area (CSA) was evaluated by both 2D and 3D echocardiography, providing two complementary approaches for determining the effective LVSV.

Assessment of LVEDV, LVESV and LVSV by anatomical M-mode:

LVEDVM-Mode, LVESVM-Mode, and LVSVM-Mode were calculated in the standardized parasternal long-axis (pLAX) view using anatomical M-Mode. To avoid LV secant sectional planes, appropriate alignment was ensured by preliminary biplane parasternal scanning. Measurements included LV internal diameter, interventricular septum thickness, and posterior wall thickness in both diastole (LVIDd, IVSd, LVPWd) and systole (LVIDs, IVSs, LVPWs). The LV remodeling index (LVRI) was derived from the ratio of LV mass (LVM) to LVEDV, while ejection fraction (LVEF) was calculated as: LVEF = [(LVEDV − LVESV) / LVEDV] × 100%.

Speckle tracking echocardiography:

Apical four-chamber, two-chamber (2-CH), and long-axis views were obtained using harmonic imaging of three consecutive end-expiratory cardiac cycles at high frame rates (>70 frames/sec). Grayscale images of the LV from these views were analyzed offline with 2D speckle-tracking echocardiography (2D-STE). The endocardial border was manually traced at end-systole, after which the software automatically tracked the myocardial region of interest and generated strain curves for each segment. Longitudinal strain (LS) was measured in the basal, mid, and apical inferior septal and anterolateral segments from the apical four-chamber view; in the basal, mid, and apical inferior and anterior wall segments from the apical 2-CH view; and in the basal, mid, apical anterior, and inferolateral wall

segments from the apical long-axis view. Global longitudinal strain (GLS) was then calculated as the average strain of all 17 LV segments.

STATISTICAL ANALYSIS

SPSS version 25.0 was used for data processing in order to verify, enter, and analyze the data. The normality of data distribution was assessed using the Shapiro–Wilk test. The student "t" test, Mann Whitney test, Fisher exact test, Chi-square test (X2), Pearson correlation, univariate logistic analysis, and multivariate regression analysis were among the statistical techniques employed.

RESULTS

The demographic data reveals statistically non-significant difference in age between women with and without subclinical systolic dysfunction, with means of 52.00 years (SD ± 6.81) and 52.04 years (SD ± 7.04) respectively (p = 0.986). However, diabetes mellitus (DM) was statistically significantly more prevalent among those with dysfunction (55.6%) compared to those without (25.0%) (p = 0.036). There were no statistically significant differences were observed in other risk variables, such as smoking, obesity, hypertension, and dyslipidemia (**Table 1).**

There were no statistically significant difference in Pre-exercise hs-TnT between patients with/without subclinical systolic dysfunction. High-sensitivity troponin T (hs-TnT) levels were significantly elevated in individuals with subclinical systolic dysfunction after exercise. Post-exercise levels further reinforced this finding, with means of 20.68 ng/L (SD ± 9.20) versus 12.23 ng/L (SD ± 8.30) (p = 0.002). The increase in troponin was also significant (15.89 ng/L vs. 9.20 ng/L, p = 0.008) (**Table 2).**

The dysfunction group had a substantially higher basal diastolic blood pressure (p = 0.023) and a nearly significant peak diastolic blood pressure (p = 0.055). Additionally, there were notable differences in heart rate responses, with the dysfunction group exhibiting considerably greater peak heart rates (p = 0.008). (**Table 1S).**

Evaluation of left ventricular (LV) characteristics showed that there were no appreciable variations in EF, IVsed, or LVPWed across the groups. However, those with subclinical dysfunction had a substantially higher left atrial volume index (LAVI) (33.64 mL/m², SD ± 6.42 vs. 28.30 mL/m², SD ± 7.37; p = 0.011). Additionally, the E/e' ratio was significantly higher in the dysfunction group (13.36, SD ± 3.99 vs. 9.77, SD ± 4.70; p = 0.007). Global longitudinal strain (GLS) analysis revealed a significant reduction in women with subclinical systolic dysfunction, with a mean of 14.22% (SD ± 1.48) compared to 21.10% (SD ± 2.22) in those without (p < 0.001). The strain rate (SRE) showed no significant difference (p = 0.374) (**Table 3).**

The TIMI risk grade analysis indicates a significant relationship between TIMI grades and subclinical systolic dysfunction. Interestingly, TIMI grade 1 was assigned to 18.5% of patients with subclinical systolic dysfunction, whereas TIMI grade 2 was assigned to 70.4% of patients. On the other hand, 85.0% of individuals without dysfunction were classified as TIMI grade 3 (p < 0.001). (**Table 4).**

The correlation analysis reveals significant associations between global longitudinal strain (GLS) and several clinical parameters. both basal diastolic blood pressure (DBP) (r = -0.396, p = 0.006) and left atrial volume index (LAVI) (r = -0.459, p = 0.001) exhibited strong negative correlations with GLS. The E/e' ratio also demonstrated a significant negative correlation (r = -0.502, p < 0.001). Conversely, age and heart rate did not show significant correlations with GLS (**Table 5).**

The analysis of heart rate (HR) increase and exercise duration demonstrated several noteworthy correlations. A strong positive correlation was observed between HR increase and left atrial volume index (LAVI) (r = 0.748, p < 0.001), alongside a similarly strong correlation with the E/e' ratio (r = 0.764, p < 0.001). Conversely, GLS exhibited a significant negative correlation with HR increase (r = -0.413, p = 0.004), indicating that higher HR responses are associated with impaired myocardial strain. Exercise duration showed a positive correlation with GLS (r = 0.301, p = 0.040), suggesting that longer exercise duration may be linked to better myocardial function (**Table 2S).**

Post-exercise increasing in troponin exhibited a significant association with an odds ratio (Exp(B)) of 1.122 (p = 0.013), suggesting that the risk of subclinical impairment increases with each unit increase in troponin levels. The E/e' ratio, LAVI, and HR rise were among the other parameters that did not provide significant predictive value (p > 0.05) (**Table 6).**

The area under the curve (AUC) for post-exercise troponin increase was 0.743 (95% CI: 0.594 to 0.859), indicating good predictive accuracy for identifying subclinical systolic dysfunction. A cutoff point of >12.6 ng/L was established, yielding a sensitivity of 70.37% and specificity of 75.00% (p = 0.0015) (**Table 7, figure 2S).**

Table (1): Comparison between women with/without subclinical systolic dysfunction regarding Demographic and Clinical Characteristics

	subclinical systolic dysfunction				P value
	No (n=21		Yes (n=27)		
	Mean	SD	Mean	SD	
Age	52.00	6.81	52.04	7.04	0.986
	N	%	N	%	
Smoking	4	20.0%	9	33.3%	0.598
Obesity	2	10.0%	8	29.6%	0.244
HTN	9	45.0%	16	58.3%	0.352
DM	5	25.0%	15	55.6%	0.036
Dyslip.	9	45.0%	10	37.0%	0.582

Table (2): Comparison between women with/without subclinical systolic dysfunction regarding Exercise duration and Post-exercises' Troponin changes

	subclinical systolic dysfunction				P value
	No		Yes		
	Mean	SD	Mean	SD	
Pre-EST hs-TnT	3.46	1.98	4.49	1.75	0.062
Post-EST hs-TnT	12.23	8.30	20.68	9.20	0.002
Troponin increase	9.20	7.60	15.89	8.68	0.008
P value	<0.001		<0.001		
Exercise duration	467.40	64.13	430.67	85.48	0.114

Table (3): Comparison between women with/without subclinical systolic dysfunction regarding Echocardiographic parameters, strain and longitudinal function.

	subclinical systolic dysfunction				P value
	No		Yes		
	Mean	SD	Mean	SD	
EF	62.44	4.19	61.70	4.37	0.567
IVSed	10.90	1.21	10.96	0.98	0.845
LVPWed	10.65	0.99	10.59	0.89	0.836
LVEDV	99.00	10.37	102.30	11.20	0.309
LVESV	37.10	3.71	38.41	4.13	0.269
LAVI	28.30	7.37	33.64	6.42	0.011
E/e'	9.77	4.70	13.36	3.99	0.007
SRE	0.39	0.17	0.34	0.21	0.374
GLS (%)	-21.10	2.22	-14.22	1.48	<0.001

Table (4): Comparison between women with/without subclinical systolic dysfunction regarding TIMI grades

TIMI grade	subclinical systolic dysfunction				p value
	No		Yes		
1	0	0.0%	5	18.5%	<0.001
2	3	15.0%	19	70.4%	
3	17	85.0%	3	11.1%	

Table (5): Correlation between GLS and various parameters

Age	r	-0.112
	P value	0.455
SBP Basal	r	-.292*
	P value	0.046
DBP Basal	r	-.396**
	P value	0.006
HR Basal	r	-0.040
	P value	0.788
Exercise duration	r	.301*
	P value	0.040
EF	r	0.012
	P value	0.937
IVSed	r	-0.039
	P value	0.792
LVPWed	r	-0.020
	P value	0.893
LVEDV	r	-0.230
	P value	0.119
LVESV	r	-0.157
	P value	0.293
LAVI	r	-.459**
	P value	0.001
E/e'	r	-.502**
	P value	<0.001
SRE	r	0.139
	P value	0.353
TIMI grade	r	.631**
	P value	<0.001

Table (6): Prediction with subclinical systolic dysfunction

	Exp(B)	95% C.I.for EXP(B)		Sig.
		Lower	Upper	
Troponin increase	**1.122**	**1.025**	**1.229**	**0.013**
HR increase	**1.006**	**0.947**	**1.069**	**0.853**
LAVI	**0.959**	**0.695**	**1.323**	**0.799**
E/e'	**1.263**	**0.737**	**2.165**	**0.395**
DM	**3.205**	**0.812**	**12.639**	**0.096**

Table (7): Accuracy of post-exercise Troponin increasing in predicting subclinical systolic dysfunction

	AUC	95% CI	Cut-off point	Youden index J	Sensitivity	Specificity	P
Troponin increase	**0.743**	**0.594 to 0.859**	**>12.6**	**0.4537**	**70.37**	**75.00**	**0.0015**

DISCUSSION

Diabetes was substantially more common in patients with dysfunction in the current investigation, even though age did not statistically significantly differ across groups. (55.6% vs. 25.0%, p = 0.036), with no other significant risk factor differences.

Our study can be supported by Sara et al. **[11]** who discovered that 50.4 years was the average age. In females with non-obstructive CAD and chest discomfort, those with microvascular dysfunction had significantly higher HbA_{1c} ($7.4 \pm 2.1\%$ vs $6.5 \pm 1.1\%$, $p = 0.035$) and fasting glucose (144 ± 56 mg/dL vs 122 ± 28, $p = 0.035$)—highlighting the association between diabetes and subclinical dysfunction.

Additionally, a Japanese registry by Fujita et al. **[12]** revealed that the probability of HF hospitalization was 1.26 times greater for women with diabetes and CAD than for men (95% CI 1.06–1.50). The patients were 67.6 years old on average. This aligns with our finding that subclinical systolic dysfunction is more common among diabetic women.

Moreover, a study by Ghoreyshi-Hefzabad et al. **[13]** using 2D speckle-tracking echocardiography reported that higher BMI and presence of diabetes independently predicted impaired LV systolic function.

Diabetes-induced coronary microvascular dysfunction and myocardial remodeling may account for the increased incidence of subclinical systolic dysfunction in diabetic women with non-obstructive CAD. Chronic hyperglycemia leads to endothelial dysfunction, reduced nitric oxide availability, and microvascular rarefaction, impairing myocardial perfusion despite unobstructed epicardial arteries. Additionally, insulin resistance and metabolic dysregulation promote oxidative stress, inflammation, and interstitial fibrosis, whereby, even when the ejection fraction is retained, all lead to decreased strain and poor myocardial deformation **[14]**.

In the current study, pre-exercise hs-TnT levels did not differ significantly between patients with and without subclinical systolic dysfunction, post-exercise levels were significantly higher in those with dysfunction (20.68 ± 9.20 ng/L vs. 12.23 ± 8.30 ng/L, p = 0.002), with a greater rise in troponin as well (15.89 ng/L vs. 9.20 ng/L, p = 0.008).

Kastner et al. **[15]** reported that the greater post-exercise rise in hs-TnT among patients with subclinical systolic dysfunction may be attributed to impaired myocardial mechanics and microvascular dysfunction, which increase cardiomyocyte susceptibility to stress-induced injury. During exercise, elevated wall stress

and limited microvascular perfusion in dysfunctional myocardium can cause transient ischemia, increased membrane permeability, or low-grade myocyte damage, leading to enhanced troponin release. This reflects an early pathophysiological response in vulnerable myocardium, even in the absence of obstructive coronary artery disease.

Peak diastolic pressure in our study trended toward significance (p = 0.055), and baseline diastolic pressure was significantly higher in patients with subclinical systolic dysfunction (p = 0.023). Furthermore, the dysfunction group's peak heart rate was noticeably greater (p = 0.008).

Our study is consistent with Bjorkavoll-Bergseth et al. **[16]** He stated that patients with CAD had higher systolic (p = 0.001) and diastolic (p = 0.002) blood pressure readings obtained at the summit of the most challenging hill.

The higher baseline diastolic pressure and peak heart rate in patients with subclinical systolic dysfunction likely reflect increased vascular resistance and heightened sympathetic activation. Elevated diastolic pressure raises afterload, increasing myocardial wall stress and impairing myocardial relaxation and contractile efficiency. Similarly, an exaggerated heart rate response during exercise may indicate autonomic dysregulation and reduced cardiovascular reserve, both of which can worsen myocardial strain and contribute to early systolic dysfunction despite preserved ejection fraction **[17]**.

In the current study, there was no significant differences were found in EF, IVsed, or LVPWed between groups, patients with subclinical systolic dysfunction had significantly higher LAVI (33.64 ± 6.42 vs. 28.30 ± 7.37 mL/m², p = 0.011) and E/e' ratio (13.36 ± 3.99 vs. 9.77 ± 4.70, p = 0.007).

In agreement with our study Bjorkavoll-Bergseth et al. **[16]** revealed that 13 out of 64 (20%) INOCA participants had greater left atrial stiffness, a sign of early atrial remodeling in women with INOCA. When they compared the left atrial volume index (LAVI) of INOCA patients and controls, they found that INOCA patients had significantly higher values in all phases: reservoir (30.4 ± 5.5 vs. 23.7 ± 3.3 mL/m², P <.05), conduit (24.4 ± 4.9 vs. 18.8 ± 2.8 mL/m², P <.05), and booster (17.9 ± 4.0 vs. 13.9 ± 2.4 mL/m², P <.05), indicating affected atrial function.

Cho et al. **[18]** found that whereas women had greater E/e′, there was no significant difference in e′ velocity or PASP (E/e′: $10.6\% \pm 3.8\%$ vs. $9.3\% \pm 2.5\%$, $p < 0.001$). Of the components of LVDD, women were more likely to have an E/e′ ratio of >14 and left atrial enlargement [118, 51.3% vs. 71, 26.4%, $p < 0.001$] and an E/e′ ratio >14 [63, 21.0% vs. 18, 6.1%, $p < 0.001$] respectively.

Patients with subclinical systolic dysfunction may have underlying diastolic dysfunction with elevated left ventricular filling pressures, as indicated by elevated LAVI and E/e′ ratios. Impaired myocardial relaxation and elevated diastolic pressures lead to chronic left atrial pressure overload, resulting in atrial remodeling and volume enlargement. This sustained hemodynamic stress contributes to subtle myocardial strain abnormalities and reduced contractile efficiency, even when ejection fraction remains preserved, indicating an early stage of cardiac dysfunction **[19]**.

In the present study, GLS was significantly reduced in women with subclinical systolic dysfunction (14.22 ± 1.48%) compared to those without (21.10 ± 2.22%, p < 0.001), while SRE did not differ significantly between groups (p = 0.374).

This aligns with a study of patients with chest pain, no obstructive CAD, and documented coronary microvascular dysfunction (CMD) by Tagliamonte et al. **[20]** and found significantly lower resting GLS in CMD-positive patients ($-16.8 \pm 2.7\%$) versus those without CMD ($-19.1 \pm 3.1\%$, $p < 0.01$).

A study of 85 INOCA patients (49 women) using speckle-tracking echocardiography by Sucato et al. **[21]** found significantly reduced resting GLS in INOCA individuals (−16.71 %) compared to healthy controls (−19.64 %), $p = 0.003$.

Additionally, in a case-control study involving 60 patients with angina and normal coronaries by Hoque et al. **[22]** reported that GLS in the angina group was −18.78 % vs −19.70 % in controls ($p < 0.007$).

The reduced GLS in women with subclinical systolic dysfunction likely reflects early impairment of subendocardial longitudinal fibers, which are particularly susceptible to ischemia, fibrosis, and increased wall stress. These fibers contribute significantly to longitudinal contraction, and their dysfunction leads to decreased myocardial deformation despite preserved ejection fraction. The absence of a significant difference in strain rate (SRE) suggests that while the timing of contraction may be maintained, the overall contractile performance is reduced, indicating early myocardial damage at the fiber level **[23]**.

TIMI grade and subclinical systolic dysfunction were shown to be significantly correlated in our study: 70.4% of patients with dysfunction were in grade 2 and 18.5% in grade 1, while 85.0% of those without dysfunction were in grade 3 ($p < 0.001$).

A study by Sucato et al. **[21]** showed that higher TIMI frame count—a visuo-angiographic indicator of microvascular dysfunction— showed a strong correlation ($r = 0.418$, $p = 0.021$) with worse global longitudinal strain (GLS). This is similar to our discovery that particular TIMI grades correspond to worse functioning.

Another analysis in the WISE cohort by Petersen et al. **[24]** showed that elevated TIMI frame count was predictive of hospitalization for angina in women with non-obstructive CAD.

The association between lower TIMI flow grades and subclinical systolic dysfunction likely reflects underlying coronary microvascular dysfunction, which limits myocardial perfusion despite the absence of significant epicardial stenosis. Reduced TIMI grades indicate impaired blood flow, potentially due to endothelial dysfunction or microvascular spasm, leading to chronic subendocardial ischemia. This ischemia affects the subendocardial fibers responsible for longitudinal contraction, resulting in reduced myocardial strain and early systolic impairment even when ejection fraction appears preserved **[25]**.

We found that global longitudinal strain (GLS) was significantly negatively correlated with basal diastolic blood pressure ($r = -0.396$, $p = 0.006$), left atrial volume index (LAVI) ($r = -0.459$, $p = 0.001$), and the E/e' ratio ($r = -0.502$, $p < 0.001$), but not with age or heart rate. Heart rate rise was adversely correlated with GLS ($r = -0.413$, $p = 0.004$) and strongly correlated with both LAVI ($r = 0.748$, $p < 0.001$) and E/e' ratio ($r = 0.764$, $p < 0.001$), indicating worse strain with greater HR response. Additionally, exercise duration positively correlated with GLS ($r = 0.301$, $p = 0.040$), suggesting better myocardial function with longer exercise tolerance.

In concordance with our study Noori and Barzani **[26]** discovered that patients with poorly managed HT were more likely to have lower GLS (than -19%) (Odds Ratio (OR)=9). Mitral annular plane systolic excursion (MAPSE) (p=0.001), interventricular septal thickness (IVSd) (p=0.003), left ventricular mass (p=0.003), and left ventricular remodeling (p=0.02) were the traditional echocardiographic markers that predicted decreased GLS. There was a strong connection between GLS and the aortic acceleration-to-ejection time ratio (AT/ET) (p=0.034).

A study by Rhea et al. **[27]** discovered that there was an inverse relationship between SP and GLS: DP vs. GLS (r=−0.33, P=0.001); SP vs. GLS (r=−0.26, P=0.009). CAD settings that are not restrictive by Arkowski et al. **[28]**, both LAVI and E/e′ have been independently associated with lower GLS levels.

Kažukauskienė et al. **[29]** found that cardiac pressures were substantially linked with GLS, average E/e', TR velocity, LAVi, and LVEF, and that the correlation was much stronger with E/GLS than with GLS.

Furthermore, a study of ischemic heart disease patients by Zhang et al. **[30]** found significant correlations between GLS and exercise

capacity metrics (peak VO_2, METs), such that better exercise performance corresponded to higher (more negative) GLS.

The negative correlations between GLS and diastolic blood pressure, LAVI, and E/e′ ratio suggest that elevated filling pressures and impaired diastolic relaxation increase myocardial wall stress, leading to subendocardial dysfunction and reduced strain. Higher LAVI and E/e′ reflect chronic pressure overload and diastolic stiffness, which compromise subendocardial fiber performance **[31]**. The strong association between heart rate increase and both LAVI and E/e′ indicates that impaired diastolic function triggers a compensatory rise in heart rate during exercise, further straining the myocardium. The inverse relationship between heart rate rise and GLS supports this, as greater hemodynamic stress exacerbates subclinical systolic dysfunction. In contrast, longer exercise duration correlates with better GLS, reflecting preserved myocardial reserve and healthier cardiac mechanics **[32]**.

However, Lee et al. **[33]** noted that in females, age was inversely correlated with GLS. The discrepancy with our study is likely due to our younger mean age (~52 yrs) and narrower range.

In our study, post-exercise troponin increase was significantly associated with subclinical systolic dysfunction, with an odds ratio of 1.122 ($p = 0.013$), indicating that each unit rise in troponin increases the likelihood of dysfunction. In contrast, HR increase, LAVI, and the E/e' ratio were not significant predictors ($p > 0.05$).

A study of middle-aged recreational athletes by Bjorkavoll-Bergseth et al. **[16]** showed that post-exercise cTnT elevation had a steeper workload-related response in those with non-obstructive CAD than in those without.

In the WISE-CVD cohort by Quesada et al. **[34]** (women with suspected INOCA), ultra-high sensitivity troponin-I (u-hscTnT) was quantifiable in 100% of participants and significantly associated with impaired systolic strain and adverse LV remodeling, even after adjusting for confounders.

In a large ANOCA/INOCA cohort (N=556) Al-Badri et al. **[35]**, a combined biomarker score including hs-TnT predicted major adverse events and structural/functional abnormalities.

An observational study of chest pain patients without obstructive CAD by Yang et al. **[36]** discovered that poor myocardial perfusion was independently linked to elevated high-sensitivity troponin I (hs-TnT) (OR ~1.145, $p < 0.001$), suggesting that the likelihood of dysfunction increased dramatically with each unit rise in troponin.

The significant association between post-exercise troponin increase and subclinical systolic dysfunction likely reflects underlying myocardial stress or microinjury triggered by exercise in the setting of impaired myocardial reserve. In patients with subtle contractile dysfunction, exercise-induced wall stress and limited microvascular perfusion may cause transient ischemia or membrane disruption, leading to troponin leakage. This biochemical response captures early cellular injury not detected by structural or hemodynamic markers like HR increase, LAVI, or E/e′, which reflect chronic loading conditions rather than acute myocardial damage, explaining their lack of predictive value **[37]**.

The post-exercise troponin increase in our study demonstrated good predictive accuracy for subclinical systolic dysfunction, with an AUC of 0.743 (95% CI: 0.594–0.859, $p = 0.0015$). A cutoff value of >12.6 ng/L provided 70.37% sensitivity and 75.00% specificity.

The good predictive accuracy of post-exercise troponin increase for subclinical systolic dysfunction likely reflects underlying myocardial vulnerability to stress-induced injury. In patients with impaired myocardial strain, exercise imposes hemodynamic stress that may lead to transient subendocardial ischemia or increased cardiomyocyte membrane permeability, resulting in troponin leakage. This mechanism highlights the sensitivity of troponin as a marker of early myocyte injury, occurring before overt changes

in ejection fraction, and underscores its utility in detecting subtle contractile dysfunction in non-obstructive CAD **[38]**.

CONCLUSION

Our study concludes that subclinical systolic dysfunction in women with non-obstructive coronary artery disease is substantially correlated with myocardial injury, as indicated by higher post-exercise troponin-I levels. More than half of the patients had impaired global longitudinal strain despite preserved ejection fraction, underscoring the value of advanced echocardiographic assessment for early detection of subtle myocardial dysfunction. Importantly, post-exercise troponin elevation emerged as a predictor of dysfunction with good diagnostic accuracy, adding incremental value beyond established tools such as the Duke Treadmill Score and strain imaging. These findings highlight the clinical importance of integrating functional assessments with biomarker testing into the diagnostic workup of women with angina and no obstructive CAD, thereby enhancing risk stratification and guiding more timely management.

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Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interest

Limitations:

This study has important limitations. It was conducted at a single center with a modest, female-only sample, which may restrict generalizability. The observational design precludes causal inference, and coronary microvascular function was not directly assessed. Furthermore, the short follow-up period did not capture long-term outcomes. Future multicenter studies with larger, more diverse populations, extended follow-up, and advanced assessments of coronary microvascular function are warranted to validate and expand upon these findings.

REFERENCES

1. Pitliya A, AlEdani EM, Bhangu JK, Javed K, Manshahia PK, Nahar S, et al. The impact of elevated troponin levels on clinical outcomes in patients with acute ischemic stroke: a systematic review. Ann Indian Acad Neurol 2023;26(5):641–54.
2. Bucciarelli-Ducci C, Ostenfeld E, Baldassarre LA, Ferreira VM, Frank L, Kallianos K, et al. Cardiovascular disease in women: insights from magnetic resonance imaging. Eur Heart J Cardiovasc Imaging 2020;21(7):707–18.
3. Bergström G, Persson M, Adiels M, Björnson E, Bonander C, Ahlström H, et al. Prevalence of subclinical coronary artery atherosclerosis in the general population. Circulation 2021;144(12):916–29.
4. Waheed N, Elias-Smale S, Malas W, Maas AH, Sedlak TL, Tremmel J, et al. Sex differences in non-obstructive coronary artery disease. Cardiovasc Res 2020;116(4):829–40.
5. Jalnapurkar S, Landes S, Wei J, Mehta PK, Shufelt C, Minissian M, et al. Coronary endothelial dysfunction appears to be a manifestation of a systemic process: a report from the Women's Ischemia Syndrome Evaluation–Coronary Vascular Dysfunction (WISE-CVD) study. PLoS One 2021;16(9):e0257184.
6. Rodriguez Lozano PF, Rrapo Kaso E, Bourque JM, Morsy M, Taylor AM, Villines TC, et al. Cardiovascular imaging for ischemic heart disease in women: time for a paradigm shift. JACC Cardiovasc Imaging 2022;15(8):1488–501.
7. Lopez-Pais J, Coronel BI, Gil DG, Pascual MJ, Durán BA, Peredo CGM, et al. Clinical characteristics and prognosis of myocardial infarction with non-obstructive coronary arteries: a prospective single-center study. Cardiol J 2022;29(5):798–806.
8. Pratiti R, Sud P, Yousef M, Moza A. Cardiovascular effects of ranolazine and the scope for translational research: a current review of literature. Front Cardiovasc Drug Discov 2022;6:1–53.
9. Mark DB, Shaw L, Harrell FE Jr, Hlatky MA, Lee KL, Bengtson JR, et al. Prognostic value of a treadmill exercise score in outpatients with suspected coronary artery disease. N Engl J Med 1991;325(12):849–53.
10. Ungerer JPJ, Tate JR, Pretorius CJ. Discordance with 3 cardiac troponin I and T assays: implications for the 99th percentile cutoff. Clin Chem 2016;62(8):1106–14.
11. Sara JD, Taher R, Kolluri N, Vella A, Lerman LO, Lerman A. Coronary microvascular dysfunction is associated with poor glycemic control amongst female diabetics with chest pain and non-obstructive coronary artery disease. Cardiovasc Diabetol 2019;18(1):22.
12. Fujita Y, Morimoto T, Tokushige A, Ikeda M, Shimabukuro M, Node K, et al. Women with type 2 diabetes and coronary artery disease have

a higher risk of heart failure than men, with a significant gender interaction between heart failure risk and risk factor management: a retrospective registry study. BMJ Open Diabetes Res Care 2022;10(2):e002707.
13. Ghoreyshi-Hefzabad SM, Jeyaprakash P, Vo HQ, Gupta A, Ozawa K, Pathan F, et al. Subclinical systolic dysfunction detected by 2D speckle tracking echocardiography in adults with diabetes mellitus: systematic review and meta-analysis of 6668 individuals with diabetes mellitus and 7218 controls. Int J Cardiovasc Imaging 2023;39(5):977–89.
14. Bojer AS, Sørensen MH, Madsen SH, Broadbent DA, Plein S, Gæde P, et al. Early signs of myocardial systolic dysfunction in patients with type 2 diabetes are strongly associated with myocardial microvascular dysfunction independent of myocardial fibrosis: a prospective cohort study. Diabetol Metab Syndr 2024;16(1):41.
15. Kastner T, Frohberg F, Hesse J, Wolfarth B, Wuestenfeld JC. Exercise-induced troponin elevation in high-performance cross-country skiers. J Clin Med 2024;13(8):2335.
16. Bjorkavoll-Bergseth M, Erevik C, Kleiven Ø, Wiktorski T, Auestad B, Skadberg Ø, et al. The relationship between workload and exercise-induced cardiac troponin elevations is influenced by non-obstructive coronary atherosclerosis. Scand J Med Sci Sports 2024;34(5):e14667.
17. Epelde F. Impact of exercise on physiological, biochemical, and analytical parameters in patients with heart failure with reduced ejection fraction. Medicina 2024;60(12):2017.
18. Cho DH, Kim MA, Choi J, Kim MN, Park SM, Kim HL, et al. Sex differences in the relationship between left ventricular diastolic dysfunction and coronary artery disease: from the Korean Women's Chest Pain Registry. J Womens Health 2018;27(7):912–19.
19. Kockskaemper J, Pluteanu F. Left atrial myocardium in arterial hypertension. Cells 2022;11(19):3157.
20. Tagliamonte E, Sperlongano S, Montuori C, Riegler L, Scarafile R, Carbone A, et al. Coronary microvascular dysfunction affects left ventricular global longitudinal strain response to dipyridamole stress echocardiography: a pilot study. Heart Vessels 2023;38(4):470–7.
21. Sucato V, Novo G, Madaudo C, Di Fazio L, Vadalà G, Caronna N, et al. Longitudinal strain analysis and correlation with TIMI frame count in patients with ischemia with no obstructive coronary artery (INOCA) and microvascular angina (MVA). J Clin Med 2023;12(3):819.
22. Hoque MS, Ahmed CM, Osmany DEMMF, Sowdagar MNH, Banerjee SK. Evaluation of subclinical left ventricular systolic dysfunction by global longitudinal strain using 2D speckle tracking echocardiography in angina with normal epicardial coronary arteries. J Asian Pac Soc Cardiol 2023;2:e30.
23. Atici A, Asoglu R, Barman HA, Sarikaya R, Arman Y, Tukek T. Multilayer global longitudinal strain assessment of subclinical myocardial dysfunction related to insulin resistance. Int J Cardiovasc Imaging 2021;37(2):539–46.
24. Petersen JW, Johnson BD, Kip KE, Anderson RD, Handberg EM, Sharaf B, et al. TIMI frame count and adverse events in women with no obstructive coronary disease: a pilot study from the NHLBI-sponsored Women's Ischemia Syndrome Evaluation (WISE). PLoS One 2014;9(5):e96630.
25. He M, Han W, Shi C, Wang M, Li J, He W, et al. A comparison of dynamic SPECT coronary flow reserve with TIMI frame count in the treatment of non-obstructive epicardial coronary patients. Clin Interv Aging 2023;18:1831–9.
26. Noori AA, Barzani MA. Predictors of impaired left ventricular global longitudinal strain in patients with essential hypertension and preserved ejection fraction. Open Cardiovasc Med J 2022;16:1–8.
27. Rhea IB, Rehman S, Jarori U, Choudhry MW, Feigenbaum H, Sawada SG. Prognostic utility of blood pressure-adjusted global and basal systolic longitudinal strain. Echo Res Pract 2016;3(1):17–24.
28. Arkowski J, Obremska M, Sareło P, Wawrzyńska M. Moderately increased left ventricular filling pressure suggesting early stage of heart failure with preserved ejection fraction in patients with invasively assessed coronary microvascular dysfunction. J Clin Med 2024;13(22):6841.
29. Kažukauskienė I, Balčiūnaitė G, Baltrūnienė V, Čelutkienė J, Maneikienė VV, Čibiras S, et al. Left ventricular global longitudinal strain predicts elevated cardiac pressures and poor clinical outcomes in patients with non-ischemic dilated cardiomyopathy. Cardiovasc Ultrasound 2021;19(1):21.
30. Zhang S, Liu Y, Jiang L, Wang Z, Liu W, Zuo H. Diagnostic accuracy of global longitudinal strain for detecting exercise intolerance in patients with ischemic heart disease. J Cardiovasc Dev Dis 2022;10(1):10.
31. Bonanni F, Caciolli S, Berteotti M, Grasso Granchietti A, Tozzetti V, Cenni N, et al. Left ventricular diastolic dysfunction predicts global

longitudinal strain recovery after surgical aortic valve replacement. Diagnostics 2024;14(19):2176.
32. Robinson S, Ring L, Oxborough D, Harkness A, Bennett S, Rana B, et al. The assessment of left ventricular diastolic function: guidance and recommendations from the British Society of Echocardiography. Echo Res Pract 2024;11(1):16.
33. Lee KY, Kim HL, Kim KJ. Sex difference in the age-related decline of global longitudinal strain of left ventricle. Sci Rep 2023;13(1):18441.
34. Quesada O, Elboudwarej O, Nelson MD, Al-Badri A, Mastali M, Wei J, et al. Ultra-high sensitivity cardiac troponin-I concentration and left ventricular structure and function in women with ischemia and no obstructive coronary artery disease. Am Heart J Plus 2022;13:100115.
35. Al-Badri A, Tahhan AS, Sabbak N, Alkhoder A, Liu C, Ko YA, et al. Soluble urokinase-type plasminogen activator receptor and high-sensitivity troponin levels predict outcomes in nonobstructive coronary artery disease. J Am Heart Assoc 2020;9(8):e015515.
36. Yang N, Zhang R, Zhao C, Sun B, Wang B, Song Y, et al. Association between troponin elevation and decreased myocardial blood flow reserve in patients without obstructive coronary artery disease. Cardiology 2024;149(1):40–50.
37. Janssen S, Lamers SK, Vroemen WHM, Denessen EJS, Berge K, Bekers O, et al. Cardiac troponin concentrations following exercise and the association with cardiovascular disease and outcomes: rationale and design of the prospective TREAT cohort study. BMJ Open Sport Exerc Med 2024;10(2):e002070.
38. Erevik CB, Kleiven Ø, Frøysa V, Bjørkavoll-Bergseth M, Chivulescu M, Klæboe LG, et al. Exercise-induced cardiac troponin I elevation is associated with regional alterations in left ventricular strain in high-troponin responders. J Am Heart Assoc 2024;13(16):e034382.

Table (S1): Comparison between women with/without subclinical systolic dysfunction regarding Hemodynamic Responses for Exercise

	subclinical systolic dysfunction				P value
	No		Yes		
	Mean	SD	Mean	SD	
SBP Basal	119.30	26.30	124.04	9.01	0.388
SBP Peak	156.10	11.64	158.85	16.27	0.523
SBP increase	36.80	30.71	34.81	18.15	0.783
P value	<0.001		<0.001		
DBP Basal	76.70	4.50	80.37	5.81	0.023
DBP Peak	87.70	4.40	91.15	6.85	0.055
DBP increase	11.00	3.76	10.78	3.58	0.838
P value	<0.001		<0.001		
HR Basal	71.85	5.81	73.22	6.02	0.437
HR Peak	158.00	14.76	169.81	14.28	0.008
HR increase	86.15	17.03	96.59	15.07	0.031
P value	<0.001		<0.001		

Table (2S): Correlation between HR increase, Exercise duration and various parameters

		HR increase	Exercise duration
Age	r	0.207	0.011
	P value	0.163	0.941
EF	r	-0.039	0.168
	P value	0.793	0.260
IVSed	r	0.042	0.053
	P value	0.779	0.721
LVPWed	r	-0.010	0.079
	P value	0.945	0.599
LVEDV	r	0.067	0.057

		HR increase	Exercise duration
	P value	0.654	0.705
LVESV	r	0.022	-0.097
	P value	0.881	0.516
LAVI	r	.748**	-.698**
	P value	<0.001	<0.001
E/e'	r	.764**	-.683**
	P value	<0.001	<0.001
SRE	r	0.195	0.055
	P value	0.188	0.714
GLS (%)	r	-.413**	.301*
	P value	0.004	0.040
TIMI grade	r	-0.174	.299*
	P value	0.241	0.041

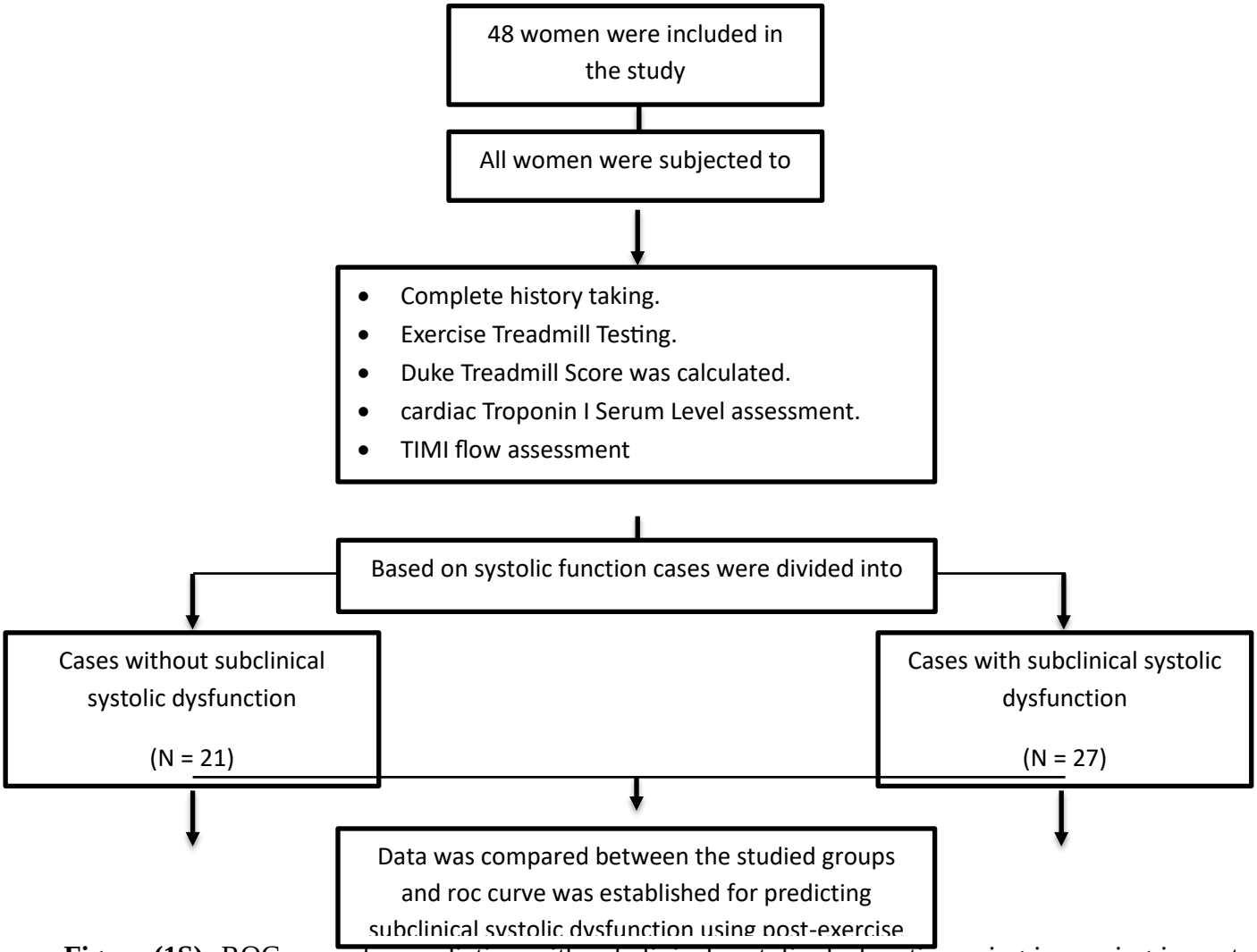

Figure (1S): ROC curve for prediction with subclinical systolic dysfunction using increasing in post-exercise Troponin.

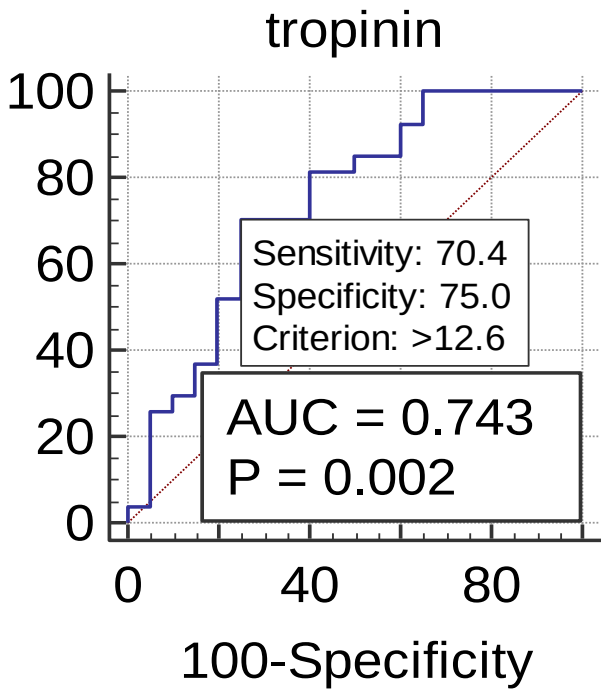

Figure (2S): ROC curve for prediction with subclinical systolic dysfunction using increasing in post-exercise Troponin.

Citation

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