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Subclinical Cardiac Dysfunction in Patients with Major Depressive Disorder

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ABSTRACT

Background: Depression is highly prevalent in cases with cardiovascular diseases (CVD), and prior studies have displayed depression as an independent risk factor for developing CVD.

Aim: To evaluate the subclinical cardiac dysfunction in patients with major depressive disorders (MDD).

Methods: This observational cross-sectional study included 82 adult patients aged 18–65 years diagnosed with major depressive disorder. Depression severity was assessed using the Beck Depression Inventory (BDI), and patients underwent thorough clinical evaluation, conventional 2D echocardiography, Tissue Doppler Imaging (TDI), and Speckle Tracking Echocardiography (STE) to detect early myocardial dysfunction.

Results: Most patients showed moderate to severe depression levels. A significant proportion was on Selective Serotonin Reuptake Inhibitors (SSRIs), with some also receiving tricyclic antidepressants, antipsychotics, and anxiolytics. There were significant associations between depression severity and specific echocardiographic parameters, including interventricular septum thickness and e′ lateral velocity, suggesting early diastolic dysfunction. Patients using tricyclic antidepressants and antipsychotics showed statistically significant variations in left ventricular (LV) dimensions and diastolic indices. A significant negative correlation between depression severity and peak A-wave velocity indicated diastolic dysfunction.

Conclusion: This study identified subclinical cardiac dysfunction in patients with major depressive disorder, shown by changes in interventricular septum thickness and e′ lateral velocity linked to depression severity. Use of tricyclic antidepressants, anxiolytics, and antipsychotics was associated with distinct cardiac changes.

Keyword: Depression, Cardiovascular Diseases, Speckle Tracking Echocardiography, Antidepressants, Antipsychotics.

INTRODUCTION

Depression is common in cases with cardiovascular disease (CVD), and 14% - 50% of patients with CVD have some degree of depression [1,2]. Preceding studies have displayed that subjects with depressive symptoms are at an increased risk of developing coronary artery disease (CAD) [3,4]. Additionally, depression has been demonstrated to be a predictor of poor prognosis in cases with pre-existing heart disease, comprising congestive heart failure, atrial fibrillation (AF), angina pectoris and myocardial infarction [5-7].

Although the pathobiological mechanism linking depression with CVD hasn't been totally elucidated, it appears likely that several biobehavioral pathways are comprised in the connections between these disease entities. Together with biobehavioral pathways, it has been hypothesized that cardiac structural or functional changes might precede the development of symptoms in cases with depression [8].

Considering that LV diastolic dysfunction is the initial step in the ischemic cascade and the earliest manifestation of diverse cardiomyopathy, it is possible that subclinical LV diastolic dysfunction could be noticed in cases with depression. On the other hand, a limited number of studies have assessed the relationship between LV systolic/diastolic function and depression using conventional two-dimensional (2D) echocardiography [9].

Essentially, TDI has developed as a promising modality for the early detection of myocardial systolic and diastolic dysfunction together with its use as a prognosticator for CVD. Till now, no epidemiological data has assessed the relation between depression and LV functional changes using TDI [10].

AIM OF WORK

The aim of the study was to evaluate the subclinical cardiac dysfunction in patients with major depressive disorders.

PATIENTS AND METHODS

This observational cross-sectional study was held at specialized Medical Hospital (Cardiology and Psychiatry departments) Mansoura University over one year. We included 82 adult male and female patients aged 18-65 years with major depressive disorder, but we excluded patients with established cardiovascular diseases as arrhythmia including AF, congenital heart disease (CHD), preceding cardiac surgeries, valvular heart disease, regional wall motion abnormality in either ventricle, and LV ejection fraction<50%, with hypertension (HTN), with diabetes mellitus (DM) and with malignant neoplasm.

METHODS

All cases were subjected to full history taking including personal history (age, sex, occupation, residence, smoking), family history of similar condition, history of medical diseases (HTN, DM, arrhythmia, dyslipidemia, thyroid disorders, and chronic kidney disease), history of previous interventions or surgery and history of medications and antiarrhythmic drugs.

Mini-International Neuropsychiatric Interview is a short structured diagnostic interview, developed for

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DSM-5 (Diagnostic and Statistical Manual of Mental Disorders, 5th edition) [11] and ICD-11 (International Classification of Diseases, 11th Revision)[12] psychiatric disorders. Depressive manifestations were evaluated by using the BDI-II questionnaire Arabic version to assess depression levels [13].

Clinical examination included general examination to assess blood pressure, pulse, respiratory rate, presence of lower limb oedema, congested neck veins and basal lung crepitation. Local cardiac examination was done to assess heart sounds, added sounds and murmurs.

Conventional 2D echocardiography was done to evaluate any malfunction or damage accompanied by the heart tissue or valves like clots, blockage, CHD, and issues such as CAD. It is a non-invasive procedure with no side effects. Tissue Doppler Imaging (TDI), which uses Doppler principles, was used to measure the velocity of myocardial motion.

Speckle tracking echocardiography is an echocardiographic imaging approach was also used. It analyses the motion of tissues in the heart by using the naturally happening speckle pattern in the myocardium to determine early myocardial dysfunction. The speckle pattern is a mixture of interference patterns and natural acoustic reflections. In addition, these reflections are defined as speckles. The pattern being random, each myocardial area has a distinctive speckle pattern that permits the region to be tracked. The speckle pattern is comparatively stable, at least from one frame to the next. In post processing this could be tracked successively frame to frame and eventually resolved into angle-independent 2D and 3D strain-based sequences. Such sequences offer quantitative and qualitative data with regard to tissue deformation and motion.

Statistical Analysis

Data analysis was conducted by SPSS software, version 26(SPSS Inc., PASW statistics for windows version 26. Chicago). Qualitative data were described using number and percent. Quantitative data were described using mean±SD for normally distributed data after testing normality using Kolmogrov-Smirnov test. Significance of the results obtained was judged at the (0.05) level. Chi-Square test was used to compare qualitative data between groups as appropriate. One way ANOVA test and Student t test were used to compare more than 2 independent groups and between 2 independent groups for normally distributed data. Spearman correlation was detected to correlate between continuous nonparametric variables.

Ethical Considerations

Approval was taken from Mansoura University Institutional Ethics Committee to achieve this study. An informed and written consent was taken from each patient. All cases were informed about the study design. The Helsinki Declaration was followed throughout the course of the investigation.

RESULTS

Table **(1)** demonstrates that mean age of studied cases was 44.98±9.74 years ranged from 24 to 60 years, 75.6% were females, 19.5% were working, 4.9% were smokers, and 69.5% had no associated medical disorders. Regarding used drugs; 100% were using SSRI and 53.7% antipsychotic drugs.

Table (1): Sociodemographic characteristics and used drugs of studied cases

	N =82	**%**
Age/years		
Mean ±SD	44.98±9.74	
(Min-Max)	(24-60)	
Sex		
Male	20	24.4
Female	62	75.6
Occupation		
Not working	66	80.5
Working	16	19.5
Smoking		
Negative	78	95.1
Positive	4	4.9
Medical History		
negative	56	69.5
Hypothyroidism	8	9.8
Hyperthyroidism	9	11
Bronchial asthma	8	9.8
Drugs		
Selective Serotonin Reuptake	82	100.0
Inhibitors (SSRI)	14	17.1
Tricyclic antidepressants	9	11.0
Anxiolytics-hypnotics	44	53.7
Antipsychotics		

SD: standard deviation

Table **(2)** illustrates a significant association between degree of depression and age of studied cases with more severe depression that was detected among younger age groups. No significant association was found between degree of depression and sex, occupation, smoking and medical history.

There was a significant association between depression grade and e lateral velocity (mms) and Interventricular Septum (IVS) cm. Mean interventricular septum (IVS) was higher among borderline clinical depression followed by severe and the least for moderate depression. Mean e lateral velocity was higher among moderate depression followed by severe and the least for borderline clinical depression.

Table (2): Relation between depression severity and socio-demographic characters and echocardiographic characters among studied cases

	Depression			**Test of significance**	**P value**
	Borderline clinical depression N=4	Moderate N=49	Severe N=29		
Age/years Mean ±SD	56.5±4.44	43.57±11.28	45.76±5.55	3.628	0.03*
Sex					
Male	3(75)	11(22.4)	6(20.7)	5.87	0.053
Female	1(25)	38(77.6)	23(79.3)		
Occupation					
Not working	2(50)	39(79.6)	25(86.2)	2.99	0.224
Working	2(50)	10(20.4)	4(13.8)		
Smoking					
Negative	4(100)	45(91.8)	29(100)	2.83	0.243
Positive	0	4(8.2)	0		
Medical History					
Negative	4(100)	32(65.3)	21(72.4)		
Hypothyroidism	0	4(8.2)	4(13.8)	8.76	0.188
Hyperthyroidism	0	9(18.4)	0		
Bronchial asthma	0	4(8.2)	4(13.8)		
Echocardiographic characters					
Left Ventricular End Diastolic Dimension (LVEDD) cm Mean ±SD	4.95±0.57	4.93±0.52	4.72±0.33	1.896	0.157
Left Ventricular End Systolic Dimension (LVESD) cm Mean ±SD	2.95±0.3	3.22±0.38	3.13±0.38	1.175	0.314
Interventricular Septum (IVS) cm Mean ±SD	1.03±0.32	0.896±0.13	0.969±0.12	3.443	0.037*
Ejection Fraction (EF)	65.0±2.71	62.86±5.54	61.93±5.82	0.632	0.534
Fractional Shortening (FS) Mean ±SD	34.25±3.3	33.36±4.19	33.38±4	0.088	0.916
Left Atrium diameter LA (cm) Mean ±SD	3.33±0.25	3.37±0.31	3.47±0.37	0.946	0.393
Aorta diameter AoR (cm) Mean ±SD	2.95±0.17	2.84±0.29	2.78±0.36	0.744	0.478
Peak E wave velocity (mms) Mean ±SD	0.618±0.06	0.717±0.14	0.661±0.14	2.058	0.135
Peak A wave velocity (mms) Mean ±SD	0.595±0.10	0.633±0.12	0.595±0.09	1.059	0.352
E/A ratio Mean ±SD	1.06±0.20	1.12±0.27	1.11±0.18	0.124	0.883
e Lateral Velocity (mms) Mean ±SD	0.103±0.015	0.131±0.03	0.117±0.01	4.001	0.022*
e Septal Velocity (mms) Mean ±SD	0.078±0.005	0.111±0.03	0.112±0.03	2.535	0.086
LV Speckle tracking longitudinal Strain Mean ±SD	-15.52±1.16	-17.64±2.78	-18.40±1.52	2.92	0.060

Used test: One Way ANOVA test, Chi-Square test, *statistically significant, SD: Standard deviation

Table (**3)** demonstrates statistically significant relation between using tricyclic antidepressants with lower mean interventricular septum (IVS) cm, lower mean peak E wave velocity (mms), mean E/A ratio, mean e lateral velocity (mms), mean e septal velocity (mms) and mean LV speckle tracking longitudinal strain.

Table (3): Relation between tricyclic antidepressants and echocardiographic characters among studied cases

	Tricyclic antidepressants		**Test of significance**	**P value**
	No (n=68)	Yes (n=14)		
Left Ventricular End Diastolic Dimension (LVEDD) cm	4.87±0.48	4.81±0.40	0.456	0.650
Left Ventricular End Systolic Dimension (LVESD) cm	3.19±0.39	3.12±0.25	0.600	0.550
Interventricular Septum (IVS) cm	0.953±0.14	0.807±0.08	3.68	0.001*
Ejection Fraction (EF)	63±5.99	60.86±1.41	1.32	0.189
Fractional Shortening (FS)	33.58±4.41	32.57±0.93	0.854	0.396
Left Atrium diameter LA (cm)	3.37±0.34	3.56±0.25	1.95	0.053
Aorta Diameter AoR (cm)	2.83±0.34	2.80±0.09	0.317	0.752
Peak E Wave Velocity (mms)	0.724±0.13	0.536±0.07	5.23	0.001*
Peak A Wave Velocity (mms)	0.622±0.12	0.596±0.09	0.736	0.464
E/A Ratio	1.16±0.23	0.898±0.054	4.13	0.001*
e Lateral Velocity (mms)	0.129±0.03	0.101±0.02	3.61	0.001*
e Septal Velocity (mms)	0.114±0.03	0.088±0.01	3.15	0.002*
LV Speckle Tracking Longitudinal Strain	-18.28±2.35	-15.48±0.95	4.36	0.001*

Data are presented as mean standard deviation (SD), Used test: Student t test, *statistically significant

Table **(4)** shows a statistically significant relation between using anxiolytics-hypnotics with lower mean interventricular septum (IVS) cm, lower mean E/A ratio, mean e lateral velocity (mms) and lower mean e septal velocity (mms).

Table (4): Relation between anxiolytics-hypnotics and echocardiographic characters among studied cases

	Anxiolytics-hypnotics		**Test of significance**	**P value**
	NO (n=73)	YES (n=9)		
Left Ventricular End Diastolic Dimension (LVEDD) cm	4.84±0.49	5.01±0.105	1.02	0.311
Left Ventricular End Systolic Dimension (LVESD) cm	3.19±0.39	3.06±0.05	1.02	0.310
Interventricular Septum (IVS) cm	0.944±0.14	0.80±0.02	2.94	0.004*
Ejection Fraction (EF)	62.46±5.64	64±4.74	0.782	0.437
Fractional Shortening (FS)	33.21±4.06	35.11±3.68	1.34	0.184
Left Atrium Diameter LA (cm)	3.41±0.34	3.38±0.26	0.237	0.814
Aorta Diameter AoR (cm)	2.82±0.32	2.88±0.21	0.537	0.592
Peak E Wave Velocity (mms)	0.695±0.15	0.669±0.06	0.521	0.604
Peak A Wave Velocity (mms)	0.619±0.12	0.599±0.13	0.502	0.617
E/A Ratio	1.14±0.23	0.91±0.047	2.87	0.005*
e Lateral Velocity (mms)	0.121±0.03	0.151±0.036	3.12	0.002*
e Septal Velocity (mms)	0.107±0.028	0.131±0.04	2.35	0.02*
LV Speckle Tracking Longitudinal Strain	-17.85±2.45	-17.41±2.26	0.516	0.608

Data are presented as mean standard deviation (SD), Used test: Student t test, *statistically significant

Table **(5)** shows a statistically significant relation between using antipsychotics with lower mean LVEDD cm, left ventricular end systolic dimension (LVESD) cm, aorta diameter AoR (cm), peak A wave velocity (mms). However; statistically significant relation was detected between using antipsychotics with higher mean peak E wave velocity (mms) and E/A ratio.

Table (5): Relation between antipsychotics and echocardiographic characters among studied cases.

	Antipsychotics		**Test of significance**	**P value**
	No (N=38)	Yes (N=44)		
Left Ventricular End Diastolic Dimension (LVEDD)cm	5.08±0.54	4.66±0.29	4.51	0.001*
Left Ventricular End Systolic Dimension (LVESD) cm	3.31±0.39	3.06±0.33	3.07	0.003*
Interventricular Septum (IVS) cm	0.939±0.16	0.918±0.14	0.660	0.511
Ejection Fraction (EF)	62.32±3.76	62.91±6.74	0.481	0.632
Fractional Shortening (FS)	32.52±2.51	34.18±4.91	1.88	0.064
Left Atrium Diameter LA (cm)	3.44±0.33	3.37±0.33	0.878	0.383
Aorta Diameter AoR (cm)	2.98±0.35	2.69±0.20	4.62	0.001*
Peak E Wave Velocity (mms)	0.655±0.14	0.725±0.13	2.31	0.024*
Peak A Wave Velocity (mms)	0.645±0.12	0.594±0.11	2.02	0.047*
E/A Ratio	1.04±0.28	1.18±0.15	2.62	0.01*
e Lateral Velocity (mms)	0.125±0.02	0.125±0.03	0.03	1.00
e Septal Velocity (mms)	0.103±0.02	0.116±0.03	1.92	0.06
LV Speckle Tracking Longitudinal Strain	-17.35±2.56	-18.20±2.23	1.60	0.112

Data are presented as mean standard deviation (SD), Used test: Student t test, *statistically significant

Table **(6)** shows statistically significant negative correlation was detected between depression score and Peak A-wave velocity (r=-0.441). Table **(7)** shows that peak A-wave velocity (mm/s) was a significant predictor of depression score in cases with major depressive disorder (MDD). Specifically, the regression coefficient (β) for peak A-wave velocity was -15.59, which was statistically significant. The negative sign of the regression coefficient suggests that as the peak A-wave velocity decreases, the depression score tends to increase, which means there was an inverse relationship between these two variables. The magnitude of β (-15.59) indicates the strength of this association. For each unit decrease in peak A-wave velocity (mm/s), the depression score is expected to increase by 15.59 points. The 95% confidence interval (CI) for the β coefficient ranged from -25.35 to -5.84. The 95% confidence interval does not include zero, reinforcing the significance and precision of the estimate.

Table (6): Correlation between depression score and echocardiographic findings of studied cases

		Depression score
Left Ventricular End Diastolic Dimension (LVEDD) (cm)	R	-.217
	P	0.051
Left Ventricular End Systolic Dimension (LVESD) (cm)	R	0.124
	P	0.267
Interventricular Septum (IVS) (cm)	R	0.145
	P	0.194
Ejection Fraction (EF%)	R	-0.175
	P	0.116
Fractional Shortening (FS%)	R	-0.143
	P	0.200
Left Atrium diameter (LA) (cm)	R	0.199
	P	0.073
Aorta diameter (AoR) (cm)	R	-0.183
	P	0.099
Peak E-wave velocity (mm/s)	R	-0.212
	P	0.056
Peak A-wave velocity (mm/s)	R	**-0.441**
	P	**0.001***
E:A ratio	R	0.008
	P	0.941
E Lateral Velocity (mm/s)	R	0.008
	P	0.944
E Septal Velocity (mm/s)	R	0.116
	P	0.301
LV Speckle tracking (longitudinal Strain)	R	-0.121
	P	0.279

r: Spearman correlation coefficient, *statistically significant

Table (7): Predictors of depression score (linear regression)

	B	P value	95%CI of β
Peak A-wave velocity (mm/s)	**-15.59**	**0.002***	**-25.35, -5.84**

B: regression coefficient, *statistically significant, CI: confidence interval.

DISCUSSION

This study investigated subclinical cardiac dysfunction among patients with MDD, with a particular focus on echocardiographic changes and the influence of antidepressant medications. The mean age of subjects was 44.83 ± 9.67 years (range: 24–60 years), with 75.6% being female. This aligns with epidemiological data suggesting higher MDD prevalence in females, potentially due to hormonal, psychosocial, and genetic factors [14].

In this study, all patients (100%) were receiving SSRIs**,** which aligns with current clinical guidelines recommending SSRIs as the first-line pharmacological treatment for major depressive disorder (MDD) due to their favorable safety and tolerability profiles [15]. A smaller proportion of patients were also prescribed tricyclic antidepressants (TCAs) (17.1%)**,** reflecting their continued use in cases where patients are non-responsive to SSRIs or have comorbid conditions such as chronic pain syndromes. However, TCAs are accompanied by a higher risk of cardiotoxicity, including arrhythmias and conduction abnormalities, which may be relevant to the observed subclinical cardiac dysfunction in this cohort [16]**.**

Moreover, 11% of the studied patients were using anxiolytics or hypnotics, typically employed to address comorbid anxiety or sleep disturbances that frequently coexist with depression. These agents, particularly benzodiazepines, have known sedative and respiratory effects but their long-term cardiovascular implications are still under investigation [17]. Notably, more than half of the patients (53.7%) were also prescribed antipsychotic medications, possibly reflecting the use of atypical antipsychotics as augmentation therapy in treatment-resistant depression. Atypical antipsychotics are known to have adverse metabolic and cardiovascular effects, including QT prolongation, weight gain, and dyslipidemia, all of which may contribute to subclinical myocardial strain and diastolic dysfunction observed in MDD populations [18]**.**

Our study revealed that younger patients demonstrated significantly higher depressive severity, with moderate and severe groups averaging 43.57 ± 11.28 and 45.76 ± 5.55 years respectively, compared to 56.5 ± 4.44 years in the borderline group ($p = 0.03$). This came in agreement with recent findings showing that early-onset depression in younger adults is often linked to elevated pro-inflammatory cytokines which include IL-1β and TNF-α**,** indicating a more biologically active form of the disorder [19]. Furthermore, new research on subclinical depression in younger adults demonstrates that symptom networks may manifest more intensely or differently in this age group, particularly in relation to anxiety, sleep, and somatic symptoms [20]. On the other hand, no significant correlation was noticed between depression severity and sex, occupation, smoking status, or medical history ($p = 0.053$, 0.224, 0.243, and 0.188, respectively). These findings are consistent with broader epidemiological data showing that, while factors like sex and smoking may contribute to depression risk, they do not consistently predict depression severity when controlling for biological age and physiological comorbidities [21].

Our study identified a significant relationship between depression severity and specific echocardiographic parameters, particularly interventricular septal (IVS) thickness and e′ lateral velocity. Patients with borderline clinical depression exhibited the highest mean IVS thickness (1.03 ± 0.32 cm), compared to those with severe (0.969 ± 0.12 cm) and moderate depression (0.896 ± 0.13 cm; $p = 0.037$). Conversely, e′ lateral velocity was highest among patients with moderate depression (0.131 ± 0.03 m/s), followed by severe (0.117 ± 0.01 m/s), and was lowest in borderline cases (0.103 ± 0.015 m/s; $p = 0.022$). These findings suggest that early subclinical diastolic changes are associated with increasing depression severity. Similar results were recorded in the literature. In a study by **Tudoran *et al.*** [22] patients with recurrent depressive episodes showed significantly increased arterial stiffness and reduced e′ velocities, indicating a direct impact of depression severity on myocardial relaxation and diastolic function**.**

Additionally, **Mehta *et al.*** [23] found that clinically significant depressive symptoms were independently associated with reduced septal e′ velocity in a Peruvian adult population, even after adjusting for confounders such as hypertension and diabetes. These results align closely with our study's findings and reinforce the importance of diastolic indices, particularly e′ velocities, as sensitive markers of early myocardial dysfunction in patients with major depressive disorder. The elevated IVS thickness in borderline depression could be explained by autonomic imbalance, particularly increased sympathetic activity, which is known to affect myocardial structure. While traditional measures such as ejection fraction did not show significant variation across depression severities, the use of tissue Doppler imaging provided a more nuanced understanding of early cardiac changes not detectable with conventional echocardiography [24].

Our study demonstrated a statistically significant association between the use of tricyclic antidepressants (TCAs) and several parameters of subclinical cardiac dysfunction. Specifically, patients using TCAs showed significantly lower mean values of interventricular

septal thickness (IVS), peak E-wave velocity, E/A ratio, e′ lateral and septal velocities, and longitudinal strain, compared to non-users. These findings suggest early diastolic and systolic abnormalities that may not be captured by conventional measures such as ejection fraction (EF), which did not differ significantly between groups. These subtle changes imply that TCAs may contribute to latent myocardial impairment in cases with MDD, even in the absence of overt cardiovascular disease. This observation is consistent with findings from the HUNT3 Study, a large-scale population-based study conducted in Norway, which reported that individuals with a history of repeated depressive episodes exhibited lower e′ tissue Doppler velocities and worsened left ventricular longitudinal strain compared to non-depressed individuals [25].

The findings from our study displayed a statistically significant relation between the use of anxiolytics-hypnotics and altered echocardiographic parameters, particularly markers of diastolic dysfunction. Patients on anxiolytics-hypnotics demonstrated significantly lower interventricular septal (IVS) thickness (0.80 ± 0.02 cm) compared to non-users (0.944 ± 0.14 cm; $p = 0.004$). In addition, this group showed a reduced E/A ratio (0.91 ± 0.047 vs. 1.14 ± 0.23; $p = 0.005$), and notably higher e′ lateral and septal velocities ($p = 0.002$ and $p = 0.020$, respectively), indicating subtle impairments in left ventricular relaxation. These diastolic changes, while not accompanied by significant differences in ejection fraction or strain, suggest the early onset of subclinical cardiac dysfunction in these patients. Recent study explored the cardiovascular implications of long-term anxiolytic and hypnotic use, especially benzodiazepines. **Tully *et al.,*** reported that chronic benzodiazepine use may impair cardiac autonomic regulation, potentially contributing to left ventricular diastolic dysfunction, especially in patients with coexisting depression and anxiety disorders [26].

In our study, the use of antipsychotics among patients with major depressive disorder was significantly associated with alterations in several echocardiographic parameters, including lower LVEDD, Left ventricular end systolic dimension (LVESD), and aortic root diameter, as well as higher Peak E wave velocity and E/A ratio ($p < 0.05$). These changes may reflect early signs of ventricular remodeling or altered diastolic function, despite preserved ejection fraction and myocardial strain. This aligns with previous research indicating that long-term antipsychotic use particularly second-generation agents may contribute to subclinical cardiac changes through mechanisms such as autonomic imbalance, metabolic side effects, or direct myocardial effects [27]. **Meyer and Stahl** [28] also found that atypical antipsychotics can impair vascular compliance and myocardial performance, contributing to reduced aortic elasticity and ventricular filling abnormalities, which may explain the altered E/A ratio observed here. The findings suggest that echocardiographic screening may be warranted in patients receiving antipsychotic therapy, particularly those with coexisting depression, to detect subtle cardiac dysfunction at an early stage.

In this study, a significant negative correlation was demonstrated between depression severity and peak A-wave velocity ($r = -0.441$, $p = 0.001$), indicating impaired diastolic function in cases with major depressive disorder. This finding suggests that higher depression scores are associated with reduced atrial contraction velocity, reflecting early subclinical cardiac dysfunction. A recent population-based echocardiographic study by **Santiago *et al.*** [29] in Peru found that individuals with clinically significant depressive symptoms exhibited notably reduced septal e′ velocities on tissue Doppler imaging, as well as a trend toward elevated E/e′ ratios, indicating subclinical impairment in left ventricular diastolic function. These associations remained significant even after adjusting for key cardiovascular risk factors—including age, sex, BMI, smoking, blood pressure, and physical activity—supporting the hypothesis that moderate to severe depression may independently contribute to diastolic dysfunction and elevated cardiovascular risk.

These findings collectively support the hypothesis that depressive disorders negatively impact cardiac mechanics at a subclinical level, potentially through neurohormonal and autonomic dysregulation mechanisms, as described in the pathophysiology of depression-related cardiovascular disease [30]. Therefore, echocardiographic screening focusing on diastolic function parameters which include Peak A-wave velocity might be valuable for early detection of cardiac involvement in cases with MDD.

CONCLUSION

This study identified subclinical cardiac dysfunction in patients with MDD, shown by changes in interventricular septum thickness and e′ lateral velocity linked to depression severity. Use of tricyclic antidepressants, anxiolytics, and antipsychotics was associated with distinct cardiac changes. A significant negative correlation between depression severity and peak A-wave velocity indicated diastolic dysfunction.

LIMITATIONS

The study design was cross-sectional, which limit the ability to establish causal relationships between depression severity and cardiac dysfunction parameters. The sample size (n=82) may not be adequate to generalize findings to the broader population of patients with MDD. The absence of a healthy control group without depression limits the ability to definitively attribute observed cardiac changes specifically to MDD. Participants were on various psychotropic medications (e.g., SSRIs, tricyclics, antipsychotics), which may independently affect cardiac function and confound the interpretation of depression-related changes. The

sample was predominantly female (75.6%) and non-smoking (95.1%), limiting the applicability of results to male and smoking populations with MDD. The study did not assess long-term cardiac outcomes or changes over time, which would be important in understanding the progression of subclinical dysfunction. Despite the use of standard techniques, echocardiographic measurements such as speckle tracking strain and diastolic parameters can be operator-dependent and subject to inter-observer variability. Although patients with known cardiac disease were likely excluded, comorbidities such as thyroid disorders or asthma may still have had subtle effects on cardiac parameters. The study was performed in a single medical center, which may limit the diversity of the sample and thus affect the external validity of the results.

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