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Journal of Clinical Cardiology and Cardiovascular Interventions
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Research Article

Echocardiographic Study of Global Longitudinal Strain in Patients with Bipolar Disorder and Schizophrenia

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Received Date: May 31, 2023; **Accepted Date:** June 12, 2023; **Published Date:** June 19, 2023

Citation: Muammer Karakayali, Ibrahim Yagci, Inanç ARTAC, Timor Omar, İbrahim Rencuzogullari, et all (2023), Echocardiographic Study of Global Longitudinal Strain in Patients with Bipolar Disorder and Schizophrenia. *J. Clinical Cardiology and Cardiovascular Interventions*, 6(5); **DOI**:10.31579/2641-0419/325

Abstract

Background: Cardiovascular diseases are the leading cause of death in patients with bipolar disorder (BD) and schizophrenia. Studies examining cardiac structure and function in patients with BD and schizophrenia using echocardiography and cardiac strain imaging are insufficient. Moreover, despite the proven increased burden of cardiovascular disease in psychiatric diseases such as BD and schizophrenia, there is unfortunately a gap in early preventive treatment. In this study, we aimed to use echocardiographic global longitudinal strain (GLS) to compare cardiac structure and function between patients with BD, schizophrenia, and mentally healthy adults.

Methods: This study recruited 92 patients diagnosed with BD (n:47) and schizophrenia (n:45). As the control group, 53 healthy volunteers without a history of psychiatric illness were included. Transthoracic echocardiography was performed for all patients.

Results: There was no difference in GLS values between patients with schizophrenia and bipolar disorder (p: 0.862). GLS values of both groups were found to be statistically significantly lower than the healthy control group (-21.7 ±1.6 vs. -15.9 ±1.5 vs. -16.1 ±1.6, $p<0.001$).

Conclusion: As a result, decreased GLS values were found in patients with psychiatric disorders compared to the healthy group in our study. Interestingly, different GLS values were also found among patients with psychiatric disorders, with statistical significance.

Keywords: schizophrenia; bipolar disorder; speckle tracking echocardiography; global longitudinal strain; cardiovascular disorders

Introduction

Bipolar disorder (BD) is a chronic mental illness that is associated with substantial functional impairment, morbidity, and mortality [1]. Schizophrenia, characterized by psychotic symptoms and in many cases social and occupational decline, remains an aetiological and therapeutic challenge [2]. However, suicide is a major cause of premature mortality in BD, most of the excess mortality rate is due to cardiovascular disorders. The life expectancy of patients diagnosed with schizophrenia is approximately 15-20 years shorter than the general population. The most important reason for this is cardiovascular mortality [3]. Both cardiovascular diseases (CVD), including coronary artery disease, and heart failure, and CVD risk factors, including abnormal electrocardiogram (ECG) patterns and high blood pressure are prevalent amongst individuals with schizophrenia and BD [4]. Speckle tracking echocardiography (STE) is a novel diagnostic tool that can provide insight into the functionality of individual myocardial fiber layers and can be clinically utilized to assess subclinical and overt myocardial dysfunction. Specifically, global longitudinal strain (GLS) by STE is more sensitive than left ventricular ejection fraction (LVEF) by conventional 2D echocardiogram to assess myocardial dysfunction [5]. Recent studies have supported the superior prognostic role of GLS for predicting major adverse cardiac events compared to LVEF [6,7]. Taken together, these require the development of effective medical tools to identify cardiac structural and functional abnormalities in the population with BD and schizophrenia patients.

Despite the proven increased burden of cardiovascular disease in psychiatric diseases such as BD and schizophrenia, there is unfortunately a gap in early preventive treatment. There is a need for multicenter, high-population, and long-term studies on this subject. In this study, we aimed to use echocardiographic GLS to compare cardiac structure and function between patients with BD, schizophrenia, and mentally healthy adults.

Methods:

This study recruited 91 patients diagnosed with BD (n:47) and schizophrenia (n:44). As the control group, 52 healthy volunteers without a history of psychiatric illness were included.

Exclusion criteria for the study were the presence of thyroid disorders, electrolyte imbalance, coronary artery disease, congestive heart failure, pulmonary hypertension, cardiomyopathy, moderate or severe valvular disease, and implantation of a permanent or temporary pacemaker, atrial fibrillation, chronic obstructive pulmonary disease, and renal failure.

Transthoracic echocardiography was performed for all patients using a Philips HD 11 XE ultrasound machine (Andover, MA, USA).

The study protocol was approved by the local ethics committee (Ethics Committee of Kafkas University Faculty of Medicine). The authors have done respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2000, as well as the national law.

Two-dimensional tissue speckle tracking echocardiography

We conducted 2-dimensional tissue speckle tracking echocardiography to obtain cardiac strain imaging. To optimize speckle tracking, two-dimensional grey-scale harmonic images were captured at a frame rate of 60–90 frames per second. The global longitudinal strain was automatically calculated as an averaged value of the peak longitudinal strain in all three-image planes. In this study, all references to changes in the global longitudinal strain were based on absolute values according to the European Association of Cardiovascular Imaging recommendations [8]. Echocardiographic examinations in this study were conducted by an experienced board-certified cardiologist blinded to the psychiatric diagnosis. The Simpson method was used to assess left ventricular ejection fraction (LVEF) as recommended by guidelines [9]. As recommended by the American Society of Echocardiography, from the parasternal long axis, via M-mode, left ventricular end-diastolic diameter (LVEDD), the left ventricular end-systolic diameter (LVESD), interventricular septum thicknesses, and posterior wall thicknesses were measured [9]. In the apical 4-chamber view, with pulse wave Doppler, mitral peak early filling (E wave) velocity, mitral late diastolic filling (A wave) velocity, trans-mitral E/A ratio, and mitral E wave deceleration time were calculated.

Statistical analysis

Continuous variables were tested for normal distribution by the Kolmogorov-Smirnov test. We report continuous data as mean and standard deviation or median. We compared continuous variables using the Student t-test or Mann-Whitney U test between groups. Categorical variables were summarized as percentages and compared with the Chi-square test. Pearson correlation coefficients examined the degree of association between examined variables. A two-tailed p-value < 0.05 was considered significant. All statistical analyses were performed with the SPSS version 20 (SPSS, Inc., Chicago, Illinois).

Results:

A total of 141 individuals (mean age 43.2 ± 10.8 and 41.8% female) were analyzed including 52 healthy controls (mean age 42 ± 10 and 48.1% female), 42 schizophrenic patients (mean age 42 ± 10 and 25% female), and 47 BD patients (mean age 44 ± 12 and 48.9% female). The general characteristics of the patients are shown in Table 1. There was no significant difference between the groups in clinical characteristics (age, hypertension, diabetes, hyperlipidemia), hematological and biochemical parameters except female sex (25 (48.1%) vs. 11 (25%) vs. 23 (48.9%) and smoking status (14 (26.9%) vs. 24 (54.5%) vs. 17 (37%), p= 0.020).

	Healthy Control (n: 52)		Schizophrenic Patients (n: 44)		Bipolar Disorder Patients (n: 47)		p
Age (years)	42	±10	42	±10	44	±12	0.460
Sex, n (%) (Female)	25	(48.1)	11	(25)	23	(48.9)	**0.031**
Smoking, n (%)	14	(26.9)	24	(54.5)	17	(37)	**0.020**
Hypertension, n (%)	1	(1.9)	1	(2.3)	5	(10.9)	0.078
Diabetes, n (%)	9	(17.3)	4	(9.1)	3	(6.5)	0.211
Hyperlipidemia, n (%)	24	(46.2)	16	(36.4)	15	(32.6)	0.366
Hemoglobin (g/dL)	14.7	±1.7	15.1	±2.0	14.7	±1.5	0.385
Glucose (mg/dL)	105.3	±35.2	100	±27.7	100	±27.4	0.613
Creatine (mg/dL)	0.7	±0.2	1	±0.2	0.7	±0.2	0.113
Total cholesterol (mg/dL)	187.5	(160-223.5)	173	(148.1-203)	160	(145-194)	0.052
LDL-C (mg/dL)	114.42	±36.75	103,82	±40.16	100.84	±36.80	0.186
HDL-C (mg/dL)	46.9	±10.8	43.6	±10	45.1	±11.1	0.328

Abbreviations: LDL-C: Low-Density Lipoprotein Cholesterol, HDL-C: High-Density Lipoprotein Cholesterol.

Table 1: Comparison of demographic and psychiatric variables between patients with bipolar disorder, schizophrenic and healthy controls.

The echocardiography values of the study population are given in Table 2. There was no significant difference between the groups in left ventricular ejection fraction (LVEF), left ventricular end diastole diameter (LVEDD), left ventricular end-systole diameter (LVESD), interventricular septum diameter (IVSD), posterior wall diameter (PWD) and mitral valve E/A ratio. GLS values were found to be lower in BD and schizophrenia patients compared to the healthy control group, which is statistically significant among the groups (-21.7 ±1.6 vs. -15.9 ±1.5 vs. -16.1 ±1.6, p<0.001).

There was no difference in GLS values between patients with schizophrenia and bipolar disorder (p: 0.862). GLS values of both groups were found to be statistically significantly lower than the healthy control group (p: <0.001).

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	Healthy Control (n: 52)		Schizophrenic Patients (n: 44)		Bipolar Disorder Patients (n: 47)		p
LVEF (%)	65	±4	64	±3	65	±4	0.367
LVEDD (mm)	47	±4	48	±5	48	±4	0.295
LVESD (mm)	31	±4	32	±5	32	±5	0.571
IVSD (mm)	9	±1	9	±1	9	±1	0.479
PWD (mm)	7.6	±1.1	7.6	±1	7.6	±1.2	0.997
Mitral valve E/A ratio	1.1	±0.2	1.2	±0.4	1.1	±0.3	0.307
LV GLS (%)	-21.7	±1.6	-15.9	±1.5	-16.1	±1.6	**<0.001**

Abbreviations: LVEF: Left Ventricular Ejection Fraction, LVEDD: Left Ventricular End Diastole Diameter, LVESD: Left Ventricular End Systole Diameter, IVSD: Interventricular Septum Diameter, PWD: Posterior Wall Diameter, LV GLS: Left Ventricular Global Longitudinal Strain.

Table 2: Echocardiographic properties of the study population and healthy control group

Discussion:

To the best of our knowledge, this is the first study to compare BD and schizophrenia patients with tissue speckle tracking echocardiography (echocardiographic GLS) in the evaluation of cardiac structure and function among themselves and with a healthy control group. The main finding of our study was that it was associated with decreased GLS values in patients with BD and schizophrenia patients compared to the healthy group. However, no significant difference was found between BD and schizophrenia patients in terms of GLS values.

In human cardiac muscles, subepicardial and subendocardial fibers are oriented in clockwise and counter-clockwise directions, respectively [10]. Therefore, the Cardium deforms along the radial, circumferential, and longitudinal axis during the systolic phase. Among the measurement of these three deformation dimensions, longitudinal strain evaluates cardiac systolic function in the longitudinal axis and allows for a closer study of subendocardial fibers. Evidence has suggested that the subendocardial layer is most vulnerable to ischemic insults (11). Moreover, meta-analysis and large-scale epidemiological studies have illustrated that the reduced global longitudinal strain predicts the risk of future major cardiovascular events, including myocardial infarction and heart failure [12, 13]. Thus, analyses of the longitudinal strain in our study could detect subclinical changes in cardiac systolic function among BD and schizophrenia patients. In our study, it was found to be associated with decreased GLS values in patients with psychiatric disorders compared to the healthy group. Nevertheless, no significant difference was found between BD and schizophrenia patients in terms of GLS values.

Smoking and drinking behaviors have been found to influence the excess mortality of people with mental disorders [14]. Smoking status and increased risk of cardiovascular disease have also been demonstrated [15]. Smoking is one of the best-established environmental risk factors associated with the occurrence of psychotic experiences in case-control studies of schizophrenia and bipolar disorder, as well as in population-based samples [16]. In our study, it was statistically significantly higher in smoking status BD and schizophrenia patients compared to the healthy control group, which was consistent with the literature.

Several studies have shown that BD and schizophrenia patients tend to have untreated cardiovascular diseases compared with the general population [17, 18]. Inadequate treatment of cardiovascular disease is also associated with high mortality in this at-risk group of patients [19]. In particular, suboptimal care of cardiovascular disease in individuals with BD and schizophrenia may be reduced when patients are diagnosed with cardiovascular disease. Consequently, we think that echocardiographic GLS evaluation, which is a simple, accessible, and inexpensive test, will help in early diagnosis and early preventive treatment in these patient groups.

Limitations:

Our study is a single-center and the sample size in this study was small, which may limit the statistical power to detect the difference in some of the echocardiographic variables between patients and controls. In addition, the unequal distribution of female sec among the groups in our study was one of the limitations of our study.

Conclusion:

With the advantages of noninvasiveness, rapid and accurate evaluation of cardiac morphology and function, and acceptable reproducibility, echocardiography is potentially among the most suitable medical techniques used for cardiac health surveillance in patients with BD and schizophrenia patients.

In our study, decreased GLS values were found in patients with BD and schizophrenia when compared with the healthy group. We think that this may show that speckle-tracking echocardiography, which is more specific than standard echocardiographic evaluation and can show worsening in cardiac functions, can be used to detect the onset of cardiovascular disease earlier in these patient groups. Multicenter studies with larger numbers of patients are needed in this regard.

Funding: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of Interest Statement: The Authors declare that there is no conflict of interest.

Statement of Ethics: The study protocol was approved by the local ethics committee (Ethics Committee of Kafkas University Faculty of Medicine). The authors have done respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2000, as well as the national law.

Data sharing: No additional data

Contributor ship: **Authors' contributions:** M.K and I.Y have given substantial contributions to the conception or the design of the manuscript. I.A, E.G, T.O and M.A have given substantial contribution to the collection of the data. I.A and Y.K have participated mostly to statistical data analysis. M.K and I.R have participated to design, analysis and drafting of the manuscript. All authors have participated to data analysis and drafting the manuscript. All authors read and approved the final version of the manuscript. All authors contributed to the manuscript and read and approved the final version of the manuscript.

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DOI:10.31579/2641-0419/325