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Original Article

Assessment of Left Ventricular Systolic and Diastolic Functions on Echocardiography in Cirrhotic Patients

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ABSTRACT

Objective: To assess the prevalence of left ventricular (LV) systolic and diastolic function on Echocardiography (ECHO) in patients presented with liver cirrhosis.

Study Design: Analytical Cross-sectional study.

Place and Duration of Study: Armed Forces Institute of Cardiology/National Institute of Heart Diseases Rawalpindi, Pakistan, from Apr 2023 to May 2023.

Methodology: Total of n=131 liver cirrhotic patients were recruited by non-probability consecutive sampling technique. All these patients presented and diagnosed with liver cirrhosis on ultrasound, were selected. Their echocardiographic assessment was done by an experienced operator. Gathered data specially the LV diastolic and systolic function, was entered and analyzed in SPSS version-24:00. Chi-square and analysis of variance was applied to find the *p*-values for study variables in relation with severity of liver cirrhosis. *p*-value <0.05 was taken statistically significant.

Results: Out of 131 Patients, 85(64.9%) patients had liver cirrhosis for less than 5-years, 32(24.4%) had for 5-10 years and 14(10.68%) for more than 10-years. There was almost similar frequency of males and females [67(51.1%) and 64(48.9%) respectively] with mean age of 57.14±9.84 years. Statistically significant association of demographics and clinical parameters with liver cirrhosis was found ($p<0.05$) except left ventricular systolic diameter ($p>0.05$). LV diastolic dysfunction was reported in 94(71.8%) while systolic function was normal in all participants. LV diastolic dysfunction was found in 56(42.7%) as grade-I, 31(23.7%) as grade-II and 7(5.3%) cases as grade-III which was statistically significant ($p<0.001$).

Conclusion: Diastolic dysfunction is relatively more common in liver cirrhosis patients as compared to systolic function. There was significant disturbance of hemodynamic parameters in these patients.

Keywords: Deceleration time, Diastolic function, E/A ratio, Echocardiographic findings, E/e ratio, Left ventricle, Left ventricular ejection fraction, Liver cirrhosis, Systolic function.

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INTRODUCTION

Cirrhosis can be defined as tissue fibrosis in normal liver with nodules development on surface of liver, abrasive liver anatomy on ultrasound and ultimately causing disturbed vital functions performed by the normal healthy liver.[1] Chronic cardiac dysfunction characterized by compromised contractility response to stress or altered diastolic function along with abnormalities in electrophysiological findings in absence of another specifically known disease comes under the term, cirrhotic cardiomyopathy.[2,3] Functional abnormality of heart in patients with hepatic cirrhosis has been identified for over sixty years.[2,4,5] The initial variations in cardiac functions were specifically attributed to alcohol consumption and with time it has been researched and found by animal and clinical studies which lent consistency to the occurrence of definite cardiomyopathy in cirrhotic patients regardless of etiology.[2,6]

Cirrhosis exists globally in 9.4% population.[7] Cirrhosis process mainly affects the liver, metabolic function followed by other organ dysfunction. Cardiac function abnormality is one of the consequences. Most notable complications include valvular disease, systolic and diastolic function abnormality, cardiomyopathy, hyper-dynamic circulation and hemodynamic anomalies. Hemodynamic variations occurred due to activation of sympathetic nervous system along with hormonal disturbance.[8]

The readily and reliable imaging modality to diagnose the cardiac function is the echocardiography (ECHO). Customary echocardiographic indices which

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depend on different clinical parameters restrict its use in subjects suffering from hyper dynamic circula-tion but another sophisticated technique is the tissue Doppler imaging to assess the diastolic dysfunction.[9] Similarly another way to gauge is the Cardiac Magnetic Resonance Imaging (CMRI).[10]

In the progression of cirrhosis, cardiac function is affected negatively resulting in reduced patient survival and saturated complications. Identifying and exploring the predictors in cardiac involvement could benefit the health professionals in choice of drug for better prognostic and clinical outcomes.[2] Echocardiographic assessment of left ventricular function could help to stratify cirrhotic patients to select an appropriate choice of therapy such as mineralocorticoid receptor antagonists, loop diuretics, and beta blockers for their management and is supportive to manage the cirrhotic patients before the cardiac dysfunction development. However, there is lack of literature in Pakistan on cirrhotic patients developing left ventricular systolic and diastolic dysfunction. Therefore, the current study was aimed to analyze the prevalence of dysfunctional left ventricular systole and diastole in patients presenting with liver cirrhosis and the relationship of aforementioned variables.

METHODOLOGY

This Analytical Cross-Sectional study was done at, Tertiary Cardiac Care Center, Rawalpindi Pakistan. Data was collected using non-probability consecutive sampling technique from April 2023 to May 2023 after ethical approval from Institutional Ethical Review Board (IERB) under approval letter number (9/2/R&D /2023/254).

WHO calculator was used for sample size calculation, by taking 9.4% prevalence of cirrhosis,[2] keeping confidence level 95% and margin of error 5% and calculated sample was 131.

Inclusion Criteria: All the patients presented and diagnosed with liver cirrhosis on ultrasound, regardless of age and gender were selected for data collection.

Exclusion Criteria: Those patients who were prediagnosed with ischemic and other cardiomyopathies, had prior history of drug intake, such as digoxin, calcium channel blocker, Coronary Heart Disease were not included. Moreover, patients with Atrial Fibrillation, Valvular Heart Diseases, pulmonary arterial hypertension due to other cause and had any endocrinopathy were also excluded.

LV systolic function is characterized by Left Ventricular Ejection Fraction (LVEF). It is the percentage of chamber volume flows from LV into aorta in systole (called stroke volume (SV)) in relation to the blood volume at the end of diastole (EDV). LVEF calculation is as follows; $$LVEF = \frac{SV \times 100}{EDV}$$.

The simplified classification proposed by American College of Cardiology (ACC) which is in clinical use is;

Normal=LVEF 50% to 70% (Mean=60%)

Mild dysfunction=LVEF 40% to 49% (Mean=45%)

Moderate dysfunction=LVEF 30% to 39% (Mean=35%)

Severe dysfunction=LVEF less than 30%.[11]

Diastolic dysfunction was termed on the basis of E/A and E/e' ratio as calculated by the findings on echocardiography. Former is the ratio from peak blood flow velocity in early diastole phase of LV (E) to the velocity in late diastole phase (A) due to atrial contraction. Later is the ratio of early filling velocity from mitral valve measured on transmittal Doppler (E) to the velocity measured on tissue Doppler (e') in early diastole phase. Deceleration time (DT) was taken from early peak inflow velocity (E-wave) to the baseline velocity and it was graded as; Grade-I: E/A<0.8, E/e'< 8, DT>200ms; Grade-II: E/A >=0.8 (0.8-2), E/e'9-12, DT 160-200ms; Grade-III: E/A>2, E/e'>13, DT<160ms.[12]

After approval from the ethical committee, patients who were diagnosed with cirrhosis on ultrasound and fulfilling the inclusion criteria were enrolled for study. An informed written consent was taken and all individuals underwent clinical assessment, laboratory tests, echocardiography, and 12-lead ECG. An experienced operator was selected to perform echocardiograms using a Xario Prime broadband S5-1 transducer ultra-sound system. Data was saved for analysis. Measure-ments and volumes of all chambers and mass of the left ventricle were calculated following the proper protocol. Pulse-wave (PW) Doppler was used to mea-sure mitral inflow velocities in the apical four-chamber view at the end of expiration. Early diastole (E) and late diastole (A) velocities were measured at the end-expiration in apical four-chamber view by placing sample volume between the mitral leaflet tips. Tissue velocities were calculated in apical four-chamber view. Early diastole (E) and atrial filling (A) was acquired in the lateral and septal mitral annulus. The systolic function of the left ventricle was measured by Simpson's method. The diastolic function

of the left ventricle was assessed in accordance with the EAE/ASE recommendations.[13] It included evaluation of peak early (E) and late diastolic (A) mitral inflow velocities, deceleration time (DT). Diastolic dysfunction was divided into three grades depending upon the severity and systolic dysfunction was divided into mild, moderate and severe as described earlier.

A predesigned questionnaire was used to collect data of study participants. Gathered data was entered and analyzed by the computer software Statistical Package for Social Sciences (SPSS)-22:00. Categorical variables were presented as frequencies & percentages and continuous variables as Mean±standard deviation. Post stratification Chi-square and Fisher exact test was applied. ANOVA was applied to find the mean difference of contionous variables between groups. *p*-value ≤0.05 was considered statistically significant.

RESULTS

Total recruited patients were n=131 presented with liver cirrhosis and their systolic as well as diastolic dysfunction were assessed. There were total 85(64.9%) patients who had liver cirrhosis for less than 5-years, 32(24.42%) had for 5-10 years and 14(10.68%) were cirrhotic patients for more than 10-years. Post-analysis results showed almost similar frequency of males and females [67(51.1%); 64(48.9%) respec-tively] with mean age 57.14±9.84 years. In patients with <5 years history of liver cirrhosis, majority 36(42.4%) were found in age bracket of 51-60 years, whereas patients having duration of liver cirrhosis between 5-10 years and >10 years had higher frequency in between age bracket of 61-70 years [(15(46.9%) & 7(50%) respectively], with significant *p*-value ($p<0.01$). In maximum patients, viral cause was prominent 67(51.1%). Left ventricular hypertrophy was found in only 19(14.5%) patients and majority 9(64.3%) belonged to >10year liver cirrhosis group. Those patients who were suffering from liver cirrhosis for more than 10-years showed significantly low hemoglobin, low platelets, high bilirubin, higher creatinine, low deceleration time, low LV diastolic diameter, higher LV systolic diameter, high LV diastolic volume and low LVEF with mean values (9.86±0.92 g/dl; 112.00±11.60mg/dl; 1.89±0.14mg/dl 1.71±0.16 mg/dl; 164.6±18.4 ms; 46.07±5.7mm; 30.00±3.86mm; 67.78±3.3ml and 53.20±2.48 respec-tively) differing significantly among liver cirrhotic groups ($p<0.05$) with the exception of LV systolic diameter ($p>0.05$). Mean values of E/A (0.89±0.35; 1.03±0.47; 1.93±0.60) and E/e ratio (8.48±3.59; 6.89±2.14; 14.9±1.19) were also compared among three groups and revealed significant results ($p<0.001$) and comparatively high ratios in liver cirrhotic patients suffering from long time (i.e. >10-years). These findings has depicted that greater the duration of liver cirrhosis more is the hemodynamic disturbance.

Diastolic dysfunction was noted in 94(71.8%) liver cirrhotic patients. Grade-I among three groups (<5 years, 5-10years, >10 years) of liver cirrhotic patients was found in [45(52.94%) out of 85; 11(34.37%) out of 32 and none out of 14) patients respectively. Similarly grade-II and III were distributed as [7(8.24%) out of 85; 15(46.8%) out of 32; 9(64.3%) out of 14] and [0(0%) out of 85; 2(6.25%) out of 32; 5(35.7%) out of 14)] patients respectively. Systolic function was normal in all study participants. Hence, it was analyzed that all of the demographics and clinical parameters including diastolic dysfunction were statistically & significantly associated with liver cirrhosis ($p<0.05$). (Table-I)

Figure showed that patients with cirrhosis for >10-years were presented with dyspnea, abdominal distention, lower limbs swelling 9(64.28%) while for 5-10 years maximum were having solely dyspnea 16(50%) and dyspnea with abdominal distension 12(37.5%) and for <5years disease, pool of patients were presented with solely dyspnea 72(84.7%).

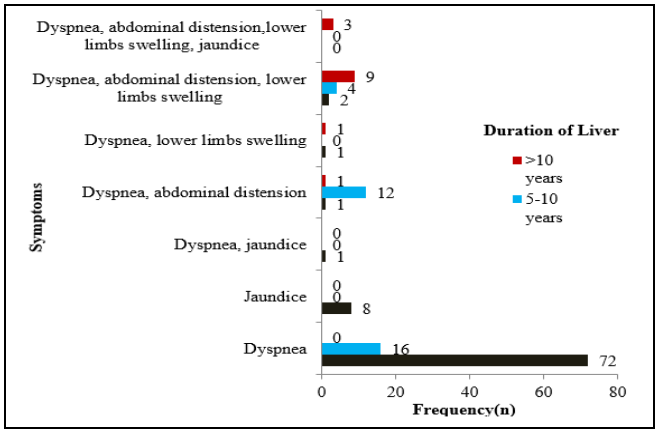

Figure: Distribution of symptoms among different groups of cirrhotic patients (n=131)

DISCUSSION

In this Analytical Cross-sectional study, preva-lence of liver cirrhosis was evaluated and association of various study variables was analyzed. Findings showed statistically significant association of all the demographic and clinical parameters with duration of cirrhosis ($p<0.05$) except LV systolic diameter.

Table-I: Association of Demographics and Clinical Parameters with Duration of Liver Cirrhosis (n=131)

Variables	(n=131)	Duration of Liver Cirrhosis; Mean±SD			*p*-value
		<5 year (n=85)	5-10 years (n=32)	>10 years (n=14)	
Gender n(%)					
Male	67(51.1)	40(47.06)	14(43.75)	13(92.8)	0.003
Female	64(48.9)	45(52.94)	18(56.25)	1(7.1)	
Age (years)					
≤50	44.70±4.61	31(36.5)	6(18.8)	-	<0.001
51-60 years	57.14±2.71	36(42.4)	10(31.3)	3(21.4)	
61-70 years	65.76±2.91	16(18.8)	15(46.9)	7(50.0)	
>70	76.00±4.58	2(2.4)	1(3.1)	4(28.6)	
Etiology of liver cirrhosis n(%)					
Alcoholic	21(16.0)	2(2.35)	9(28.12)	10(71.42)	<0.001
Viral	67(51.1)	52(61.18)	11(34.37)	4(28.57)	
Other	43(32.8)	31(36.47)	12(37.5)	0(0.0)	
Hemoglobin(g/dl) (Mean±SD)	10.85±0.94	11.06±0.82	10.65±0.95	9.86±0.92	<0.001
Platelets (x10^9 /L) (Mean±SD)	142.57±22.5	150.10±20.20	135.88±18.2	112.00±11.60	<0.001
Bilirubin(mg/dl) (Mean±SD)	1.646±0.38	1.620±0.43	1.59±0.21	1.89±0.14	0.03
Creatinine(mg/dl) (Mean±SD)	1.39±0.26	1.34±0.23	1.41±0.28	1.71±0.16	<0.001
ECG changes n(%)					
QT-Prolong	48(36.6)	20(23.53)	17(53.12)	11(78.57)	<0.001
No change	83(63.4)	65(76.47)	15(46.87)	3(21.4)	
E/A Ratio (Mean±SD)	1.03±0.52	0.89±0.35	1.03±0.47	1.93±0.60	<0.001
E/e Ratio (Mean±SD)	8.48±3.59	6.89±2.14	9.86±3.62	14.90±1.19	<0.001
Deceleration time (msec) (Mean±SD)	201.10±35.27	207.90±33.6	198.90±35.90	164.60±18.4	<0.001
Left ventricular diastolic diameter (mm) (Mean±SD)	48.29±4.07	48.17±4.0	49.59±2.70	46.07±5.7	0.02
Left ventricular systolic diameter (mm) (Mean±SD)	29.13±3.31	29.11±3.31	28.81±3.12	30.00±3.86	0.53
Left ventricular diastolic volume (ml) (Mean±SD)	62.90±4.96	62.15±4.72	62.78±5.10	67.78±3.3	<0.001
LVEF (%)	57.70±3.05	58.88±2.23	56.56±2.96	53.2±2.48	<0.001
LVH n(%)					
Yes	19(14.5)	6(7.06)	4(12.5)	9(64.3)	<0.001
No	112(85.5)	79(92.94)	28(87.5)	5(35.71)	
Diastolic dysfunction n(%)					
Grade-I	56(42.7)	45(52.94)	11(34.37)	0(0.0)	<0.001
Grade-II	31(23.7)	7(8.24)	15(46.8)	9(64.3)	
Grade-III	7(5.3)	0(0.0)	2(6.25)	5(35.7)	
Normal	37(28.2)	33(38.82)	4(12.5)	0(0.0)	
Systolic dysfunction n(%)					
Normal	131(100)	85(100)	32(100)	14(100)	-

**ECG=Electrocardiography; LVEF=Left Ventricular Ejection Fraction; LVH=Left Ventricular Hypertrophy*

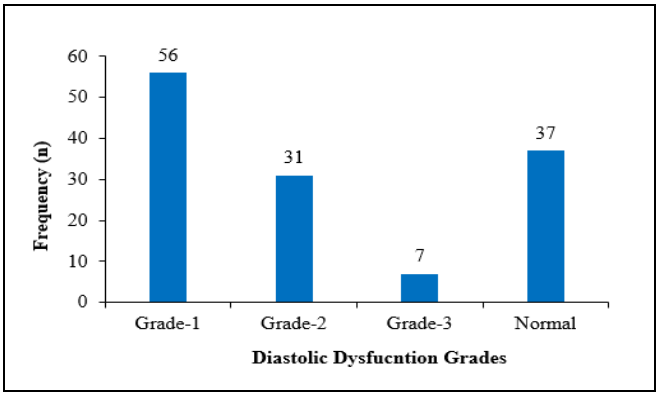

Figure-2: Distribution of diastolic Dysfunction (n=131)

Mean difference of all parameters among three study groups was also noted to be significant. Specifically, the greater the duration of liver cirrhosis a patient is suffering from, the more disturbed physiological values were. These findings were compared with past literature and revealed that their findings were also inline to our study's numeric.

Prevalence of LV diastolic dysfunction in previous studies ranged from 50-65% in liver cirrhosis patients.[14–16] LV systolic dysfunction as per the findings of a study done by Nimal *et al.* have reported to be 44.4% but with least frequency (n=4 out of 93

patients).[16] Our study has found 71.8% LV diastolic dysfunction and systolic function was normal in all study participants suffering from liver cirrhosis. In a study,[17] conducted on cirrhotic patients revealed significant age difference in cirrhotic versus non-cirrhotic patients with mean age of cirrhotic group as 57±9.1 years which is in consistent to our study's patients' mean age (57.14±9.84 years; n=131) with significant findings (p<0.01). In the same study, alcoholic etiology was noted in 53% of patients followed by 41% of viral cause to liver cirrhosis while in given study 16% were having alcoholic etiology and 51.1% viral etiology.

In another research work done by Karki *et al.*, alcoholic and non-alcoholic grouping of liver cirrhotic patients was done and significant association of diastolic dysfunction with 61.9% prevalence was reported. QT interval was relatively prolong in 79% cirrhotic patients.[14] In consistent to this, our study's evaluations demonstrated QT-prolong in higher percentage of patients (78%) having severe cirrhosis. However the prevalence of dysfunction is greater than the previously reported 50% and 65%.[15,18] This difference in numerics might be due to different study settings and population. However, in cirrhotic patient the overall cardiac function becomes com-promised with variations in physiological hemodynamics.[19,20]

Current study has reported mean of LV systolic and diastolic diameter as 29.13±3.31mm and 48.29± 4.07. Former was seen to progressively increase with severity of liver cirrhosis and later was decrease. Mean of E/A ratio was 1.03±0.52 and E/e ratio was 8.48±3.59 which showed significant increase with progression of disease (p<0.001). Rimbas *et al.* have reported almost similar result with significant findings (LV systolic diameter=33±6 mm; LV diastolic diameter =44±4 mm; E/A vs E/e ratios; 1.2±0.5, 8.7±2.1 respectively; p<0.01).[17]

Nirmal *et al.*, did cardiac function assessment by echocardiography in n=150 liver cirrhosis patients and revealed cardiac dysfunction in 51 patients with diastolic dysfunction in 42(82.3%) patients and systolic dysfunction in 9(17.64%) patients. Grade-A LV diastolic dysfunction was noted in 17 (40.5%), Grade-B was in 14(33.3%) patients and 11 (21.56%) cases were having Grade-C. LV systolic dysfunction of grade-A, grade-B and Grade-C were reported in (2, 22.2%; 4, 44.4%; and 3, 33.3% respectively) patients. These findings were also significantly related with the severity of hepatic cirrhosis (p=0.004; 0.017 respectively) and depicted various cardiac changes were due to liver cirrhosis.[16] Comparatively given study has reported normal systolic function in all study participants while diastolic dysfunction was noted in 94(71.8%) liver cirrhosis patients and greater percentage was found in patient with >10 year liver cirrhosis. Grade-A LV dysfunction was present in 56(42.7%), Grade-B was in 31(23.7%) and Grade-C was in 7(5.3%) cases with significant findings (p<0.001).

Finucci *et al.* had also demonstrated results consistent to our study with significant findings and interpreted that there is increased LV end diastolic volume (89±20 ml) of cirrhotic patients' with E/A ratio (1.02±0.35), LVEF (62±7%) and deceleration time (194±40ms).[21] Similarly current study analysis has evaluated LV end diastolic volume (62.90±4.96 ml), E/A ratio (1.03±0.52), LVEF (62.90±4.96%), and deceleration time (201.1±35.27ms) and p-value for all was <0.001.

Mortality among cirrhotic patients having comp-romised diastolic function was reported relatively high in a 22 months follow-up study which had docum-ented 44(62.9%) cases out of 70 with LV diastolic dysfunction. Of these, 16 patients died depicting lower survival rate of cirrhosis patients with LV diastolic dysfunction and findings were statistically significant (p=0.01).[22] However our study lacked follow-up to find longterm outcomes and mortality.

LIMITATIONS OF STUDY

The major limitation of current study was that it was lacked in patients' follow-up to note long-term outcomes as well as study didn't include mortality variable. Future studies could be conducted with longitudinal study designs including short and longterm complications developed in cirrhotic patients along with cardiac dysfunction to have more generalizable findings. Moreover, study was single centered and had small sample size.

CONCLUSION

Conclusively, the patients with severity of cirrhotic disease progressively have more derangements in hemodynamic parameters. Diastolic dysfunction is relatively more common in these patients as compared to systolic function.

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Conflict of Interest: None

Authors' Contribution

Following authors have made substantial contributions to the manuscript:

AY, RS & AHS: Manuscript writing, Data Analysis, Approval of the Final Version to be Published.

IA, SSK & IAK: Data analysis, Proof Reading, Approval of the Final Version to be Published.

NA & JK: Critical Review, Concept, Approval of the Final Version to be Published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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